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Serial Number: 09/007,285 Results Format Preferred (circle): PAPER DISK E-MAIL

Title of Invention _____

Inventors (please provide full names): _____

_____

Earliest Priority Date: _____

Keywords (include any known synonyms registry numbers, explanation of initialisms):

adjuvant or immunostimulant and

(dimethyldioctadecylammonium bromide.

Search Topic:

Please write detailed statement of the search topic, and the concept of the invention. Describe as specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples of relevant citations, authors, etc., if known. You may include a copy of the abstract and the broadcast or most relevant claim(s).

Point of Contact:
Mary Hale
Technical Info. Specialist
CM1 12D16 Tel: 308-4258

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 11, 2000

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Structure search limits have been increased. See HELP SLIMIT for details.

=> e dimethyldioctadeclammonium bromide/cn

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E1            1      DIMETHYLDINONYLAMMONIUM TETRAPHENYLBORATE(1-)/CN
E2            1      DIMETHYLDIOCTADECENYLAMMONIUM CHLORIDE/CN
E3            0 --> DIMETHYLDIOCTADECLAMMONIUM BROMIDE/CN
E4            1      DIMETHYLDIOCTADECYLAMMONIUM/CN
E5            1      DIMETHYLDIOCTADECYLAMMONIUM 2,5-DICHLOROBENZENESULFONATE/CN
E6            1      DIMETHYLDIOCTADECYLAMMONIUM 2,5-DIMETHYLBENZENESULFONATE/CN
E7            1      DIMETHYLDIOCTADECYLAMMONIUM
2-CHLORO-3,5-DINITROBENZENESULFO
                     NATE/CN
E8            1      DIMETHYLDIOCTADECYLAMMONIUM
2-CHLORO-5-METHYLBENZENESULFONAT
                     E/CN
E9            1      DIMETHYLDIOCTADECYLAMMONIUM
2-CHLORO-5-NITROBENZENESULFONATE
                     /CN
E10           1      DIMETHYLDIOCTADECYLAMMONIUM
2-METHYL-5-NITROBENZENESULFONATE
                     /CN
E11           1      DIMETHYLDIOCTADECYLAMMONIUM 2-NAPHTHALENESULFONATE/CN
E12           1      DIMETHYLDIOCTADECYLAMMONIUM ACETATE/CN

=> e dimethyldioctadecylammonium bromide/cn

E1            1      DIMETHYLDIOCTADECYLAMMONIUM BENZENESULFONATE/CN
E2            1      DIMETHYLDIOCTADECYLAMMONIUM BENZOATE/CN
E3            1 --> DIMETHYLDIOCTADECYLAMMONIUM BROMIDE/CN
E4            1      DIMETHYLDIOCTADECYLAMMONIUM CHLORIDE/CN
E5            1      DIMETHYLDIOCTADECYLAMMONIUM DIISOOCTYL PHOSPHATE/CN
E6            1      DIMETHYLDIOCTADECYLAMMONIUM DODECYLBENZENESULFONATE/CN
E7            1      DIMETHYLDIOCTADECYLAMMONIUM DODECYLSULFATE/CN
E8            1      DIMETHYLDIOCTADECYLAMMONIUM FLUORIDE/CN
E9            1      DIMETHYLDIOCTADECYLAMMONIUM HEPTAFLUOROBUTYRATE/CN
E10           1      DIMETHYLDIOCTADECYLAMMONIUM HYDROXIDE/CN
E11           1      DIMETHYLDIOCTADECYLAMMONIUM IODIDE/CN
E12           1      DIMETHYLDIOCTADECYLAMMONIUM METHACRYLATE/CN

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L1            1 "DIMETHYLDIOCTADECYLAMMONIUM BROMIDE"/CN



L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2000 ACS
RN   3700-67-2  REGISTRY
CN   1-Octadecanaminium, N,N-dimethyl-N-octadecyl-, bromide (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   Ammonium, dimethyldioctadecyl-, bromide (8CI)
CN   Dimethyldioctadecylammonium bromide (6CI, 7CI)
OTHER NAMES:
CN   Di-n-octadecyldimethylammonium bromide
CN   Dimethyldistearylammonium bromide
CN   Dioctadecanyldimethylammonium bromide
CN   Dioctadecyldimethylammonium bromide
CN   Distearyldimethylammonium bromide
CN   DODAB
CN   DSDMAB
CN   GERBU Adjuvant 10
CN   GERBU Adjuvant 100
DR   134821-46-8
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MF C38 H80 N . Br
CI COM
LC STN Files: AGRICOLA, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CSCHEM, DETHERM*, EMBASE, GMELIN*, IPA, MSDS-OHS, PROMT, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)
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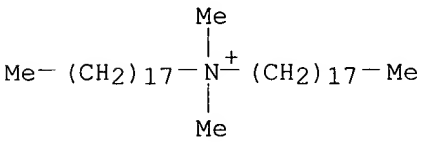

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618 REFERENCES IN FILE CA (1967 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
620 REFERENCES IN FILE CAPLUS (1967 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 132:255831 Cationic microparticles: a potent delivery system for DNA vaccines. Singh, Manmohan; Briones, Maylene; Ott, Gary; O'Hagan, Derek (Chiron Vaccines, Chiron Corporation, Emeryville, CA, 94608, USA). Proc. Natl. Acad. Sci. U. S. A., 97(2), 811-816 (English) 2000. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB An approach involving the prepn. of biodegradable microparticles with a cationic surface was developed to improve the delivery of adsorbed DNA into antigen-presenting cells after i.m. injection. The microparticles released intact and functional DNA over 2 wk in vitro. In addn., the microparticles induced higher levels of marker gene expression in vivo. After i.m. immunization, the microparticles induced significantly enhanced serum antibody responses in comparison to naked DNA. Moreover, the level of antibodies induced by the microparticles was significantly enhanced by the addn. of a vaccine adjuvant, aluminum phosphate. In addn., in contrast to naked DNA, the cationic microparticles induced potent cytotoxic T lymphocyte responses at a low dose.

REFERENCE 2: 132:252378 Modification of polypropylene fabric for giving water repellent and hygroscopic properties simultaneously. Miyazaki, Koji; Hisada, Kenji; Hori, Teruo; Watanabe, Nobuko (Faculty of Engineering, Fukui University, Fukui, 910-8507, Japan). Sen'i Gakkaishi, 55(9), 408-415 (Japanese) 1999. CODEN: SENGA5. ISSN: 0037-9875. Publisher: Sen'i Gakkai.

AB The finishing procedure for giving to polypropylene non-woven fabric water repellent and hygroscopic properties simultaneously was investigated. The high repellent property (surface tension: over 29-35 .times. 10-3 N/m) and suitable hygroscopic property (moisture content: 8-60 wt%) were obtained simultaneously by the following steps. As the first step, the hydrophilic

group was introduced into the nonwoven polypropylene fabric by radiation-induced graft polymn. of acrylic acid (AA) or mixt. of sodium p-styrene sulfonate (SSS) and AA. Hygroscopic and wettable properties were given by treating the grafted sample with sodium hydroxide soln. As the second step, polyion-complexes were formed on the sodium acrylate surface by treating with dioctadecyldimethylammonium bromide aq. soln. As a result hydrophobic surface was obtained. Then, as the third step, the alkyl chain surface was treated further with CF4-plasma treatment to give water-repellent property on that. The structure of the modified surface was analyzed after each treatment by measuring ATR-FT/IR and XPS.

REFERENCE 3: 132:251505 A topology map for novel vesicle-polymer hybrid architectures. Jung, Martin; Hubert, Dominique H. W.; Bomans, Paul H. H.; Frederik, Peter; Van Herk, Alex M.; German, Anton L. (Laboratory Polymer Chemistry Coatings Technology, Eindhoven Univ. Technology, Eindhoven, 5600 MB, Neth.). Adv. Mater. (Weinheim, Ger.), 12(3), 210-213 (English) 2000. CODEN: ADVMEW. ISSN: 0935-9648. Publisher: Wiley-VCH Verlag GmbH.

AB The concept of templating polymn. in vesicles was studied. To investigate the relationship between a surfactant/polymer combination, the reaction conditions, and the final vesicle-polymer morphol., the photopolymn. of 3 monomers (styrene, Bu methacrylate, and Bu acrylate) with different crosslinkers (ethylene glycol dimethacrylate, [3-(methacryloylamino)propyl]trimethylammonium chloride, and divinylbenzene) in dioctadecyldimethylammonium bromide and dimyristoylphosphatidylcholine vesicles was examd. The vesicle-polymer products were analyzed by cryo-transmission electron microscopy. The nanoscopic phase sepn. between surfactant matrix and polymer generally occurred for all common surfactant/polymer combinations. The individual morphol. depends on the specific interplay between vesicle-matrix and polymer. Constructive guidelines for the synthesis of novel vesicle-polymer hybrid architectures are presented.

REFERENCE 4: 132:223814 Antimicrobial treatment of polymers or dyed textiles. Sun, Gang; Kim, Young Hee (The Regents of the University of California, USA). PCT Int. Appl. WO 2000015897 A1 20000323, 34 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US20726 19990910. PRIORITY: US 1998-151891 19980911.

AB The present invention provides durable and refreshable antimicrobial polymers and methods for prepg. the same. In some instances, the polymer is a dyed textile. These textiles have excellent colorfastness and washfastness. The antimicrobial fabrics of this invention are suitable for sportswear, antiodor carpets, films, plastics, toys and medical uses. Suitable antimicrobial agents are quaternary ammonium compds., which are connected to the fabrics via colorants used in dyeing of the fabrics.

REFERENCE 5: 132:223259 Nanoscopic-Confinement Effects on Local Dynamics. Anastasiadis, S. H.; Karatasos, K.; Vlachos, G.; Manias, E.; Giannelis, E.

P. (Institute of Electronic Structure and Laser, Foundation for Research and Technology-Hellas, Crete, 71110, Greece). Phys. Rev. Lett., 84(5), 915-918 (English) 2000. CODEN: PRLTAO. ISSN: 0031-9007. Publisher: American Physical Society.

AB The segmental dynamics of 1.5-2.0 nm polymer films confined between parallel solid surfaces was studied using dielec. spectroscopy in poly(methylphenylsiloxane) (PMPS)/silicate (hectorite, montmorillonite) intercalated nanocomposites. The organically modified silicates were prepd. by cation exchange between Na silicate and dioctadecyldimethylammonium bromide and hybrids were prepd. by mixing the modified silicate with PMPS at various concns. at 60.degree. under ultrasonication to promote chain diffusion into the silicate layer. The confinement effect is evident by the observation of a mode, much faster than the bulk-polymer .alpha. relaxation and exhibiting much weaker temp. dependence. The effect is explained in terms of interlayer spacing restricting the cooperative vol. of the .alpha. relaxation or of the dominance of more mobile interphase regions as predicted by simulations; the data qual. support the former.

REFERENCE 6: 132:206693 ESAT-6 subunit vaccination against Mycobacterium tuberculosis. Brandt, Lise; Elhay, Martin; Rosenkrands, Ida; Lindblad, Erik B.; Andersen, Peter (Department of TB Immunology, Statens Serum Institut, Copenhagen, 2300, Den.). Infect. Immun., 68(2), 791-795 (English) 2000. CODEN: INFIBR. ISSN: 0019-9567. Publisher: American Society for Microbiology.

AB The ESAT-6 antigen from M. tuberculosis is a dominant target for cell-mediated immunity in the early phase of tuberculosis (TB) in TB patients as well as in various animal models. The purpose here was to evaluate the potential of ESAT-6 in an exptl. TB vaccine. The authors started out using di-Me dioctadecylammonium bromide (DDA), an adjuvant which has been demonstrated to be efficient for the induction of cellular immune responses and has been used successfully before as a delivery system for TB vaccines. Here they demonstrate that, whereas immune responses to both short-term-culture filtrate and Ag85B are efficiently induced with DDA, this adjuvant was inefficient for the induction of immune responses to ESAT-6. Therefore, the authors investigated the modulatory effect of monophosphoryl lipid A (MPL), an immunomodulator which in different combinations has demonstrated strong adjuvant activity for both cellular and humoral immune responses. The authors show here that vaccination with ESAT-6 delivered in a combination of MPL and DDA elicited a strong ESAT-6-specific T-cell response and protective immunity comparable to that achieved with M. bovis BCG.

REFERENCE 7: 132:199500 Surfactant-encapsulated clusters (SECs): (DODA)20(NH4)[H3Mo57V6(NO)6O183(H2O)18], a case study. Kurth, Dirk G.; Lehmann, Pit; Volkmer, Dirk; Colfen, Helmut; Koop, Michael J.; Muller, Achim; Du Chesne, Alexander (Max-Planck-Institute of Colloids and Interfaces, Potsdam, 14424, Germany). Chem.--Eur. J., 6(2), 385-393 (English) 2000. CODEN: CEUJED. ISSN: 0947-6539. Publisher: Wiley-VCH Verlag GmbH.

AB We present a comprehensive study of the partially reduced polyoxomolybdate [H3Mo57V6(NO)6O183(H2O)18]21- encapsulated in a shell of dimethyldioctadecylammonium (DODA) surfactant mols. Treatment of an aq. soln. of (NH4)21[H3Mo57V6(NO)6O183(H 2O)18].65H2O with a trichloromethane soln. of the surfactant leads to instant transfer of the encapsulated complex anion into the org. phase. Results from vibrational spectroscopy, anal. ultracentrifugation, small-angle X-ray scattering, transmission electron microscopy, elemental anal., and Langmuir compression isotherms are consistent with a single polyoxometalate core encapsulated within a

shell of 20 DODA mols. The molar mass of the supramol. assembly is 20249 g mol-1 and the diam. is 3.5 nm. A material with the empirical formula (DODA)20(NH4)[H3Mo57V6(NO)6O183(H2O)18] was isolated as a dark violet solid, which readily dissolves in org. solvents. Slow evapn. of soln. of 2 on solid substrates forces the hydrophobic particles to aggregate into a cubic lattice. Annealing these so-formed films at elevated temp. causes de-wetting with terrace formation similar to liq. crystals and block copolymers. (DODA)20(NH4)[H3Mo57V6(NO)6O183(H2O)18] forms a stable Langmuir monolayer at the air-water interface; Langmuir-Blodgett multilayers are readily prepd. by repeated transfer of monolayers on solid substrates. The films were characterized by optical ellipsometry, Brewster angle microscopy, transmission electron microscopy, and X-ray reflectance.

REFERENCE 8: 132:185950 Effects of added urea and alkylureas on gel to liquid-crystal transitions in DOAB vesicles. Blandamer, M. J.; Briggs, B.; Cullis, P. M.; Last, P.; Engberts, J. B. F. N.; Kacperska, A. (Department of Chemistry, University of Leicester, Leicester, LE1 7RH, UK). J. Therm. Anal. Calorim., 55(1), 29-35 (English) 1999. CODEN: JTACF7. ISSN: 1418-2874. Publisher: Kluwer Academic Publishers.

AB The gel to liq.-crystal transition for vesicles in aq. soln. formed by

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=> fil medl,caplus,biosis,embase;s (l1 or dimethyldictadecylammonium bromide) and (adjuvant or immunostimul?)

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FULL ESTIMATED COST	7.89	1185.88

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L3	67	FILE CAPLUS
L4	59	FILE BIOSIS
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L7 ANSWER 1 OF 103 CAPLUS COPYRIGHT 2000 ACS
2000:227680 Compositions and methods for WT1 specific immunotherapy. Gaiger, Alexander; Cheever, Martin (Corixa Corporation, USA). PCT Int. Appl. WO 2000018795 A2 20000406, 193 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US22819 19990930. PRIORITY: US 1998-164223 19980930; US 1999-276484 19990325.
AB Compns. and methods for the therapy of malignant diseases, such as leukemia and cancer, are disclosed. The compns. comprise one or more of a WT1 polynucleotide, a WT1 polypeptide, an antigen-presenting cell presenting a WT1 polypeptide, an antibody that specifically binds to a WT1 polypeptide; or a T cell that specifically reacts with a WT1 polypeptide. Such compns. may be used, for example, for the prevention and treatment of metastatic diseases. Such compn. may also be used for monitoring the effectiveness of immunization and therapy by detg. activation of T cell proliferation or cytolytic activity.

L7 ANSWER 2 OF 103 CAPLUS COPYRIGHT 2000 ACS
2000:82247 Document No. 132:255831 Cationic microparticles: a potent delivery system for DNA vaccines. Singh, Manmohan; Briones, Maylene; Ott, Gary; O'Hagan, Derek (Chiron Vaccines, Chiron Corporation, Emeryville, CA, 94608, USA). Proc. Natl. Acad. Sci. U. S. A., 97(2), 811-816 (English) 2000. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.
AB An approach involving the prepn. of biodegradable microparticles with a cationic surface was developed to improve the delivery of adsorbed DNA into antigen-presenting cells after i.m. injection. The microparticles released intact and functional DNA over 2 wk in vitro. In addn., the microparticles induced higher levels of marker gene expression in vivo. After i.m. immunization, the microparticles induced significantly enhanced serum antibody responses in comparison to naked DNA. Moreover, the level of antibodies induced by the microparticles was significantly enhanced by the addn. of a vaccine **adjuvant**, aluminum phosphate. In addn., in contrast to naked DNA, the cationic microparticles induced potent cytotoxic T lymphocyte responses at a low dose.

L7 ANSWER 3 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
2000:81776 Document No. 132:206693 ESAT-6 subunit vaccination against Mycobacterium tuberculosis. Brandt, Lise; Elhay, Martin; Rosenkrands, Ida; Lindblad, Erik B.; Andersen, Peter (Department of TB Immunology, Statens Serum Institut, Copenhagen, 2300, Den.). Infect. Immun., 68(2),

791-795 (English) 2000. CODEN: INFIBR. ISSN: 0019-9567. Publisher: American Society for Microbiology.

AB The ESAT-6 antigen from M. tuberculosis is a dominant target for cell-mediated immunity in the early phase of tuberculosis (TB) in TB patients as well as in various animal models. The purpose here was to evaluate the potential of ESAT-6 in an exptl. TB vaccine. The authors started out using di-Me dioctadecylammonium bromide (DDA), an **adjuvant** which has been demonstrated to be efficient for the induction of cellular immune responses and has been used successfully before as a delivery system for TB vaccines. Here they demonstrate that, whereas immune responses to both short-term-culture filtrate and Ag85B are efficiently induced with DDA, this **adjuvant** was inefficient for the induction of immune responses to ESAT-6. Therefore, the authors investigated the modulatory effect of monophosphoryl lipid A (MPL), an immunomodulator which in different combinations has demonstrated strong **adjuvant** activity for both cellular and humoral immune responses. The authors show here that vaccination with ESAT-6 delivered in a combination of MPL and DDA elicited a strong ESAT-6-specific T-cell response and protective immunity comparable to that achieved with M. bovis BCG.

L7 ANSWER 4 OF 103 CAPLUS COPYRIGHT 2000 ACS

1999:783957 Document No. 132:19228 Methods for suppressing reproductive behavior in animals using compositions containing GnRH immunogens, analogs, and antibodies. Robbins, Sarah C. (Biostar Inc., Can.). PCT Int. Appl. WO 9962545 A2 19991209, 88 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-CA493 19990528. PRIORITY: US 1998-88024 19980604; US 1999-306689 19990506.

AB Methods for achieving suppression of reproductive behavior and/or fertility in a vertebrate subject are disclosed. The methods use compns., administered prior to puberty, contg. GnRH immunogens, GnRH analogs such as GnRH agonists and antagonists, or GnRH antibodies. The methods are useful for the prolonged suppression of testicular function in males and ovarian function in females. The GnRH immunogen of the invention is a GnRH multimer comprising the general formula (GnRH-X-GnRH)y wherein: GnRH is a GnRH immunogen; X is one or more mols. selected from the group consisting of a peptide linkage, an amino acid spacer group, a carrier mol. and [GnRH]n, where n is an integer greater than or equal to 1; and y is an integer greater than or equal to 1. The carrier mol. is specifically a leukotoxin polypeptide. The compn. can further contain an immunol. **adjuvant**. The vertebrate of the invention is selected from the group consisting of a feline subject, a canine subject, an equine subject and a cervine subject.

L7 ANSWER 5 OF 103 CAPLUS COPYRIGHT 2000 ACS

1999:722921 Document No. 131:350674 Raising of animals for meat production by vaccination with GnRH immunogen. Manns, Jack G.; Acres, Stephen D.; Harland, Richard (Biostar Inc., Can.). PCT Int. Appl. WO 9956771 A2 19991111, 87 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-CA360 19990505. PRIORITY: US 1998-84217 19980505.

AB Uncastrated male animals are immunized with a primary vaccination of a GnRH immunogen which causes a redn. in circulating gonadal steroid levels, followed by revaccination with a GnRH immunogen shortly before slaughter to reduce the level of one or more androgenic and(or) nonandrogenic steroids. The methods are useful for producing cuts of meat with enhanced organoleptic qualities. Thus, bull calves vaccinated s.c. twice with GnRH immunogen at day 0 and day 56 had significant redns. in scrotal circumference by day 84 and reduced testosterone levels by day 98.

L7 ANSWER 6 OF 103 CAPLUS COPYRIGHT 2000 ACS

1999:606907 Document No. 131:241962 Tuberculosis vaccine. Andersen, Peter; Andersen, Bengaard; Haslove, Kaare; Sorensen, Anne Lund (Statens Seruminstitut, Den.). U.S. US 5955077 A 19990921, 39 pp., Cont.-in-part of U.S. Ser. No. 123,182, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-465640 19950605. PRIORITY: US 1993-123182 19930920; WO 1994-DK273 19940701.

AB The invention relates to novel secreted antigens from mycobacteria capable of evoking early (within 4 days) responses from T-helper cells in the form of gamma-interferon release in immunized animals after rechallenge infection with mycobacteria of the tuberculosis complex. The antigens are present in short term filtrates (ST-CF) from cultured mycobacteria belonging to the tuberculosis complex. One of these antigens, a polypeptide with an apparent mol. wt. of 6 kDa, has been identified, and the DNA encoding the polypeptide has been cloned and sequenced. The antigens of the invention are believed useful esp. in vaccines, but also in diagnostic compns., esp. for diagnosing infection with virulent mycobacteria.

L7 ANSWER 7 OF 103 CAPLUS COPYRIGHT 2000 ACS

1999:582580 Document No. 131:219176 **Adjuvant** formulation with enhanced immunogenic activity, and related compositions and methods. Littel-Van den Hurk, Sylvia van Drunen; Zamb, Timothy; Redmond, Mark J. (University of Saskatchewan, Can.). U.S. US 5951988 A 19990914, 8 pp., Cont. of U.S. Ser. No. 39,990, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-463837 19950605. PRIORITY: US 1993-39990 19930330.

AB **Adjuvant** formulations are provided contg. quaternary ammonium salts in conjunction with an oil component which may be a mineral oil, an animal oil, a vegetable oil, a mixt. thereof, or an oil-in-water emulsion of one or more of such oils. These formulations are useful in conjunction with known immunol. substances, e.g., viral or bacterial antigens in a vaccine compn., in order to enhance the immunogenic response. The compns. are also useful without an incorporated antigen as nonspecific **immunostimulatory** formulations.

L7 ANSWER 8 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2

1999:709851 Document No. 132:34418 Interleukin-6 and interleukin-12

participate in induction of a type 1 protective T-cell response during vaccination with a tuberculosis subunit vaccine. Leal, Irene S.; Smedegard, Birgitte; Andersen, Peter; Appelberg, Rui (Laboratory of Microbiology and Immunology of Infection, Institute for Molecular and Cell Biology, University of Porto, Oporto, Port.). Infect. Immun., 67(11), 5747-5754 (English) 1999. CODEN: INFIBR. ISSN: 0019-9567. Publisher: American Society for Microbiology.

AB The authors examd. the role of cytokines in the development of .gamma. interferon (IFN-.gamma.)-secreting protective T cells following immunization with a culture filtrate subunit vaccine against Mycobacterium tuberculosis contg. the **adjuvant** dimethyldioctadecylammonium bromide (DDA). Depletion of either interleukin-6 (IL-6) or IL-12 with specific neutralizing antibodies during vaccination reduced the priming of T cells for antigen-specific proliferation and IFN-.gamma. secretion. Such redn. was also obsd. in IL-6 gene-disrupted mice as compared to wild-type animals. IL-6 was found to play a role in the initial differentiation of Th1 cells but not in their expansion. The defect found after IL-6 depletion or in IL-6-knockout mice was compensated by the inclusion of recombinant mouse IL-12 in the vaccine. The induction of protective immunity against an i.v. or an aerosol challenge with live, virulent M. tuberculosis was markedly reduced by neutralizing either IL-6 or IL-12 during immunization with the vaccine. Likewise, the effects of IL-6 neutralization were partially reversed by including IL-12 in the vaccine. The authors' data point to an important role of IL-6 and IL-12 in the generation of cell-mediated immunity to tuberculosis.

L7 ANSWER 9 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

1999355304 EMBASE **Adjuvant** modulation of T-cell reactivity to 30-kDa secretory protein of Mycobacterium tuberculosis H37Rv and its protective efficacy against experimental tuberculosis. Sharma A.K.; Verma I.; Tewari R.; Khuller G.K.. Prof. G.K. Khuller, Department of Biochemistry, Postgrad. Inst. Med. Education Res., Chandigarh, India. Journal of Medical Microbiology 48/8 (757-763) 1999.
Refs: 28.
ISSN: 0022-2615. CODEN: JMMIAV. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The immunoprotective behaviour of the 30-kDa secretory glycoprotein of Mycobacterium tuberculosis H37Rv has been investigated in different **adjuvant** systems in two mouse strains, NMR1 and C57BL/6J. In comparison with Freund's incomplete **adjuvant** (FIA) and dimethyldioctadecyl ammonium bromide (DDA), the 30-kDa glycoprotein complexed with polylactide-co-glycolide microparticles (PLG-MPs) induced maximum immunoreactivity in the two mouse strains. As compared with controls, immunisation with 30-kDa-PLG-MPs resulted in significantly greater protection in animals challenged with 1 x LD50 of M. tuberculosis H37Rv on the basis of survival rates and number of cfu in the infected organs 30 days after challenge. The degree of protection provided by 30-kDa-PLG-MPs was similar to that obtained with 30-kDa-FIA and higher than BCG immunisation. These findings suggest that biodegradable PLG microparticles can be used as an efficient carrier system for the key immunoprotective 30-kDa secretory protein antigen of M. tuberculosis H37Rv.

L7 ANSWER 10 OF 103 CAPLUS COPYRIGHT 2000 ACS

1998:789046 Document No. 130:24104 Immunopotentiating composition. Fujioka, Keiji; Sano, Akihiko; Nagahara, Shunji; Brandon, Malcolm Roy; Nash, Andrew

Donald; Lofthouse, Shari (Sumitomo Pharmaceuticals Co., Ltd., Japan; The University of Melbourne; Koken Co., Ltd.). PCT Int. Appl. WO 9852605 A1 19981126, 80 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-JP2172 19980518. PRIORITY: JP 1997-145920 19970519; JP 1997-142461 19970530; JP 1997-316285 19971030.

AB The present invention provides an immunopotentiating compn. which comprises an antigen or antigen-inducing substance, and a carrier comprising a biocompatible material for effectively increasing an immune response derived from an antigen. The present invention further provides a method of producing an antibody by administering said immunopotentiating compn. to a mammal or bird, thereby modulating the immune response in said mammal or bird and recovering the antibody produced.

L7 ANSWER 11 OF 103 CAPLUS COPYRIGHT 2000 ACS

1998:430020 Document No. 129:94457 Method of preparing a synergistic immunological **adjuvant** formulation. Grubhofer, Nikolaus (Gerbu Biotechnik G.m.b.H., Germany). U.S. US 5773011 A 19980630, 9 pp. Cont.-in-part of U. S. 153,406, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1995-505409 19950721. PRIORITY: DE 1993-4332825 19930927; DE 1993-4333376 19930930; US 1993-153406 19931116.

AB The improved method uses N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP) or N-acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP) in low dose ranges in a combination with Zn-L-proline complex and with **immunostimulating** lipid (e.g. dimethyldioctadecylammonium bromide) in doses which synergistically potentiate the effect of each single component. The zinc-L-proline complex contains an excess of L-proline or 5-oxo-L -proline which serves as a solubilizer and dispersing agent for the lipid component. The combination provokes antibody titers that far exceed the additive effect of each individual component and also that of Freund's **adjuvant**, as shown in expts. with rabbits using bovine serum albumin as antigen.

L7 ANSWER 12 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS

1998:281604 Document No.: PREV199800281604. Influence of several **adjuvants** on the immune response against a recombinant meningococcal high molecular weight antigen. Gonzalez, S. (1); Nazabal, C.; Vina, L.; Caballero, E.. (1) Cent. Genet. Eng. and Biotechnol., P.O. Box 6162, Havana Cuba. Brown, F. [Editor]; Haaheim, L. R. [Editor]. Developments in Biological Standardization, (1998) Vol. 92, pp. 269-276. Developments in Biological Standardization; Modulation of the immune response to vaccine antigens. Publisher: S. Karger AG P.O. Box, Allschwilerstrasse 10, CH-4009 Basel, Switzerland. Meeting Info.: Symposium Bergen, Norway June 18-21, 1996 International Association of Biological Standardization. ISSN: 0301-5149. ISBN: 3-8055-6640-9. Language: English.

L7 ANSWER 13 OF 103 CAPLUS COPYRIGHT 2000 ACS

1998:649647 Document No. 130:2901 Effective, nonsensitizing vaccination with culture filtrate proteins against virulent Mycobacterium bovis infections in mice. Bosio, Catharine M.; Orme, Ian M. (Mycobacterial Research

Laboratories, Department of Microbiology, Colorado State University, Fort Collins, CO, 80523, USA). Infect. Immun., 66(10), 5048-5051 (English) 1998. CODEN: INFIBR. ISSN: 0019-9567. Publisher: American Society for Microbiology.

AB Vaccination of mice with M. bovis culture filtrate proteins (CFP), prepd. in a variety of **adjuvants** (aluminum hydroxide, Quil-A, and dimethyldioctyldecyl ammonium bromide [DDA]), provided protection against an aerosol challenge of virulent M. bovis. Addnl., vaccination with CFP in DDA or Quil-A did not sensitize mice to M. bovis purified protein deriv.

L7 ANSWER 14 OF 103 CAPLUS COPYRIGHT 2000 ACS

1998:340240 Document No. 129:121373 Influence of several **adjuvants** on the immune response against a recombinant meningococcal high molecular weight antigen. Gonzalez, S.; Nazabal, C.; Vina, L.; Caballero, E. (Center for Genetic Engineering and Biotechnology, Havana, Cuba). Dev. Biol. Stand., 92(Modulation of the Immune Response to Vaccine Antigens), 269-276 (English) 1998. CODEN: DVBSA3. ISSN: 0301-5149. Publisher: S. Karger AG.

AB Studying outer membrane proteins as vaccine candidates, the authors' group has previously isolated, cloned, and expressed in Escherichia coli the gene encoding for a high mol. wt. protein (P64k), common to many meningococcal strains. To continue the characterization of this meningococcal antigen, the authors have evaluated its immunogenicity in mice alone or combined with several com.-available **adjuvants**. The authors used as an **adjuvant** aluminum hydroxide (Alhydrogel and Rehydragel), aluminum phosphate, Algammulin, crude saponin, the saponin Quil A, dimethyl-dioctadecyl ammonium bromide (DDA), Freund's **adjuvant**, and Montanide 888. The antibody titers against the recombinant protein and whole meningococci elicited with these **adjuvants** were compared. The authors found that Quil A produced the highest titers against the recombinant P64k. Algammulin and the quaternary ammonium compd. DDA induced the highest levels of antibodies against meningococci. The authors analyzed the recognition of a set of linear peptides by antisera prepd. against the protein combined with some of the **adjuvants**. The responses depended on the **adjuvant** used and the results have been confirmed by epitope mapping using overlapping peptides synthesized on pins.

L7 ANSWER 15 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3

1998:708606 Document No. 130:236130 Effect of various **adjuvants** on secondary immune response in chickens. Hilgers, L. A. Th.; Nicolas, I.; Lejeune, G.; Dewil, E.; Boon, B. (Solvay Research and Technology, Applied Immunology, Brussels, Belg.). Vet. Immunol. Immunopathol., 66(2), 159-171 (English) 1998. CODEN: VIIMDS. ISSN: 0165-2427. Publisher: Elsevier Science B.V..

AB Stimulatory effects of several types of **adjuvants** on secondary antibody response to inactivated Newcastle disease virus (iNDV) were examd. in chickens. For this purpose, animals were primed with iNDV without **adjuvant** resulting in a low but significant antibody response, boosted with iNDV plus **adjuvant** 3 wk later, and analyzed for specific antibody titers in serum 3 wk after the booster. Water-in-mineral oil emulsion (W/O) caused significant increase in antibody titers measured in an indirect enzyme-linked immunosorbent (ELISA), hemagglutination inhibition (HI), and virus neutralization (VN) assay. The **adjuvants** tested included three oil-in-water emulsions (i.e. mineral oil-in-water, sulfolipo(SL)-Ficoll400/squalane-in-water and sulfolipo-cyclodextrin/squalane-in-water), three neg.-charged

polymers with high mol. wt. (i.e. polyacrylate, polystyrenesulfonate and sulfo(S)-Ficoll400) and two surface-active agents (i.e. dimethyldioctadecylammonium bromide (DDA) and Quil A). These **adjuvants** enhanced significantly the secondary immune response but none reached the titer obtained with W/O. Combinations of **adjuvants** with distinct physicochem. properties, i.e. polyacrylate and DDA revealed only slight, beneficial effects. We concluded that the various types of **adjuvants** tested can stimulate secondary immune responses in primed animals but that W/O is superior.

L7 ANSWER 16 OF 103 CAPLUS COPYRIGHT 2000 ACS

1998:458376 Document No. 129:243701 New **adjuvants** for boosting immune response in vaccination and antibody production. Grubhofer, Nikolaus (Gerbu Biotechnik GmbH, Gaiberg, 69251, Germany). Bioforum Int., 2(2), 90-92 (English) 1998. CODEN: BINTFQ. Publisher: GIT Verlag GmbH.

AB A review with 8 refs. Vaccination against infectious diseases should lead to formation of immunity in the host organism which is sufficient for sustained or even lifelong protection. In the past this was very well accomplished just by the administration of antigens in the form of the inactivated pathogenic organisms and it was relatively easy to prep. the required amt. of organism. The last decades however have witnessed the advent of viral infections such as hepatitis B and HIV where mass prodn. of the virus is not possible. One has to resort to genetically engineered viral subunits which are mere polypeptides and by far not as immunogenic as the whole pathogen. Repetitive injections are required and the high price is prohibitive for the badly needed mass vaccinations. An example: 350 million people worldwide are infected with the potentially fatal Hepatitis B virus. At least 1 billion protective vaccinations are required, 3 shots, each one not less than US$ 10. Therefore it becomes mandatory to increase the power of a vaccine by adding so called **adjuvants**. Prodn. of antibody for scientific or pharmaceutical purposes is an other use for **adjuvants** because very frequently the available antigens are not very immunogenic and of course high antibody yield as well as avoidance of animal losses are important economical issues here.

L7 ANSWER 17 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS

1997:515654 Document No.: PREV199799814857. Interactions between cationic liposomes and an antigenic protein: The physical chemistry of the immunoadjuvant action. Tsuruta, Lilian R.; Quintilio, Wagner; Costa, Maria H. B.; Carmona-Ribeiro, Ana M. (1). (1) Dep. Bioquimica, Instituto Quimica, Caixa Postal 26077, Sao Paulo, SP Brazil. Journal of Lipid Research, (1997) Vol. 38, No. 10, pp. 2003-2011. ISSN: 0022-2275. Language: English.

AB The 18 kDa antigenic protein from Mycobacterium leprae (P) or its N-acyl derivative (AP) was incorporated in di-octadecyldimethylammonium bromide (DODAB) liposomes in water or in phosphate-buffered saline (PBS). In water, 100% P incorporation in liposomes contrasts with 65% in PBS. There is 75-80% AP incorporation to liposomes in water against 55-65% in PBS, showing that attachment of hydrophobic residues to the protein, instead of increasing, further decreases incorporation to the liposomes. From protein adsorption on latex, P affinity is larger than AP affinity for the latex surface whereas limiting adsorption for AP is much larger than that obtained for P, possibly due to AP aggregation in solution. P-induced rupture of liposomes containing (14C)sucrose was evaluated from dialysis

of protein/liposomes mixtures. In water, P incorporation to the liposomes causes leakage of radioactive contents contrasting with the absence of leakage for P incorporation in PBS. Immunization tests for delayed type hypersensitivity indicate at enhancement of cell mediated immunological response towards P/DODAB complexes that is not obtained for the isolated protein. Absence of leakage for P in PBS is associated with a P "lying-over" on the liposome and optimization of protein presentation to the immunological system.

L7 ANSWER 18 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4
1997:97818 Document No. 126:170131 **Adjuvant** modulation of immune responses to tuberculosis subunit vaccines. Lindblad, Erik B.; Elhay, Martin J.; Silva, Regina; Appelberg, Rui; Andersen, Peter (TB Res. Unit, Statens Seruminst., Copenhagen, 2300, Den.). Infect. Immun., 65(2), 623-629 (English) 1997. CODEN: INFIBR. ISSN: 0019-9567. Publisher: American Society for Microbiology.

AB Mice were immunized with exptl. subunit vaccines based on secreted antigens from Mycobacterium tuberculosis in a series of **adjuvants**, comprising incomplete Freund's **adjuvant** (IFA), di-Me dioctadecyl ammonium bromide (DDA), RIBI **adjuvant**, Quil-A saponin, and aluminum hydroxide. Immune responses induced by these vaccines were characterized by in vitro culture of primed cells, PCR anal. for cytokine mRNA, detection of specific IgG isotypes induced, and monitoring of protective immunity to tuberculosis (TB). The study demonstrated marked differences in the immune responses induced by the different **adjuvants** and identified both IFA and DDA as efficient **adjuvants** for a TB subunit vaccine. Aluminum hydroxide, on the other hand, induced a Th2 response which increased the susceptibility of the animals to a subsequent TB challenge. DDA was further coadjuvanted with either the Th1-stimulating polymer poly(I-C) or the cytokines gamma interferon, interleukin 2 (IL-2), and IL-12. The addn. of IL-12 was found to amplify a Th1 response in a dose-dependent manner and promoted a protective immune response against a virulent challenge. However, if the initial priming in the presence of IL-12 was followed by two booster injections of vaccine without IL-12, no improvement in long-term efficacy was found. This demonstrates the efficacy of DDA to promote an efficient immune response and suggests that IL-12 may accelerate this development, but not change the final outcome of a full vaccination regime.

L7 ANSWER 19 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
1998073460 EMBASE Immunological requirements for a subunit vaccine against tuberculosis. Elhay M.J.; Andersen P.. Dr. P. Andersen, Department of TB Immunology, Statens Serum Institut, Artillerivej 5, Copenhagen 2300 S, Denmark. tbimm@ssi.dk. Immunology and Cell Biology 75/6 (595-603) 1997.

Refs: 83.
ISSN: 0818-9641. CODEN: ICBIEZ. Pub. Country: Australia. Language: English. Summary Language: English.

AB Tuberculosis remains one of the most important threats to world health. Current vaccination and prevention strategies are inadequate and there is an urgent need for a new vaccine. The current vaccine bacille Calmette-Guerin (BCG), is unable to protect against re-activation of disease in later life and its efficacy varies tremendously in different human populations. An ideal replacement would be a non-living subunit vaccine that could impart protective efficacy greater than BCG but without its drawbacks. Before such a goal is achieved, however, there are many parameters that need to be examined in experimental systems. Such studies have revealed that apart from the selection of immunologically relevant

antigens, dosage of antigen and type of **adjuvant** need to be chosen carefully. These parameters need to be examined in the context of the complex biology of the disease and, despite recent progress in defining host/pathogen interactions, experimental vaccines tested so far have fallen short of the protective efficacy of BCG. A coordinated approach, stimulating the various facets of cell-mediated immunity will probably be essential for development of protective immunity through subunit vaccination.

L7 ANSWER 20 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1998:121727 Document No.: PREV199800121727. The immune response in rabbits to bovine serum albumin together with **adjuvant** and synergists. Domkus, V. (1); Bukelskiene, V. (1); Grubhofer, N.. (1) Inst. Biochem., Vilnius Lithuania. Baltic Journal of Laboratory Animal Science, (1997) Vol. 7, No. 4, pp. 225-231. ISSN: 1407-0944. Language: English. Summary Language: English; Russian.
AB The glycopeptide N-acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP), a natural compound isolated from the cell walls of the well-known nutrient microorganism Lactobacillus bulgaricus, was tested as immunoadjuvant on rabbits. The optimal dose of GMDP as an **adjuvant** of humoral immunity was 10 mug per rabbit. The chemical compounds, as Zn proline (Zn) and dimethyldioctadecylammonium bromide (DDA), synergistically increased the **adjuvant** action in rabbits. The optimal antibody titres (15383+-12222) were obtained by subcutaneous immunization of rabbits with 100 mug bovine serum albumin (BSA) together with 10 mug GMDP+100 mug Zn+100 mug DDA. The administration of BSA antigen together with GMDP and synergists did not show any abnormal effects on the rabbit health.

L7 ANSWER 21 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
96174098 EMBASE Document No.: 1996174098. Beneficial effects of additional **adjuvants** on the immune response to haptenated liposomes. Verheul A.F.M.; Golding B.; Inman J.K.; Snippe H.. EWIMCM, Utrecht University, Academic Hospital,Utrecht, Netherlands. Journal of Liposome Research 6/2 (397-414+441-444) 1996.
ISSN: 0898-2104. CODEN: JLREE7. Pub. Country: United States. Language: English. Summary Language: English.
AB The humoral immune response to haptenated liposomes is well documented. This review summarizes our efforts in this field of research. The immunogenicity of haptens, small oligosaccharides and peptides linked to phosphatidyl ethanolamine are studied in mice. Special attention is given to the immunomodulating properties of lipid A, its derivatives and the synthetic **adjuvants** non-ionic block polymers and dimethyldioctadecylammonium bromide on the outcome of the response to these haptenated liposomes.

L7 ANSWER 22 OF 103 CAPLUS COPYRIGHT 2000 ACS
1996:267272 Document No. 124:340255 Unique immunomodulating properties of dimethyl dioctadecyl ammonium bromide (DDA) in experimental viral vaccines. Katz, D.; Lehrer, S.; Galan, O.; Lachmi, B.; Cohen, S.; Inbar, I.; Samina, I.; Peleg, B.; Heller, D.; et al. (Department of Virology, Israel Institute for Biological Research, Ness-Ziona, 74100, Israel). Adv. Exp. Med. Biol., 397(Novel Strategies in the Design and Production of Vaccines), 115-25 (English) 1996. CODEN: AEMBAP. ISSN: 0065-2598.
AB A review, with 22 refs. This paper is a summary of the authors' studies with DDA as an **adjuvant** in exptl. viral vaccines in which the immunomodulating properties of DDA are demonstrated.

L7 ANSWER 23 OF 103 CAPLUS COPYRIGHT 2000 ACS
1995:501322 Document No. 122:237772 Low-molecular-weight proteins released by mycobacteria, their manufacture with recombinant cells, and their use in diagnosis and in tuberculosis vaccines. Andersen, Peter; Andersen, Aase Bengaard; Hasloev, Kaare; Soerensen, Anne Lund (Statens Serumsinstitut, Den.). PCT Int. Appl. WO 9501441 A1 19950112, 100 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, CZ, DE, DE, DK, DK, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ, TT, UA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1994-DK273 19940701. PRIORITY: DK 1993-798 19930702.

AB The invention relates to a secreted antigenes from mycobacteria capable of evoking early (within 4 days) immunol. responses from T-helper cells in the form of .gamma.-interferon release in memory immune animals after rechallenge infection with mycobacteria of the tuberculosis complex. The antigens are present in short term culture filtrates from cultured mycobacteria belonging to the tuberculosis complex. One of these antigens, a polypeptide with an apparent mol. wt. of 6 kDa, has been identified, and the DNA encoding the polypeptide has been cloned and sequenced. Also disclosed are methods of immunizing animals/humans and methods of diagnosing tuberculosis.

L7 ANSWER 24 OF 103 CAPLUS COPYRIGHT 2000 ACS
1995:520577 Document No. 122:263525 **Adjuvant** for enhancing the yield of antibodies in immunology. Grubhofer, Nikolaus (Gerbu Biotechnik GmbH, Germany). Eur. Pat. Appl. EP 646378 A1 19950405, 6 pp. DESIGNATED STATES: R: CH, DE, DK, FR, GB, IT, LI, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1994-114233 19940909. PRIORITY: DE 1993-4333376 19930930.

AB An immune **adjuvant** which provides a stronger and more reliable immune response than prior art prepns. contains a synergistic mixt. of a glycopeptide, a Zn compd., and a quaternary ammonium salt. Thus, a soln. of Zn proline complex 2.9 g, dimethyldioctadecylammonium bromide 40 mg, and N-acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-isoglutamine (GMDP) 20 mg in 50 mL water was sterilized by filtration, dispensed in 100-.mu.L portions into tubes, and lyophilized; each tube contained sufficient **adjuvant** for 10 injections in rabbits. Other effective **adjuvant** components included Cu and Se salts, tocopheryl phosphate, isoprinosine, dextran, dextran sulfate, and CHAPS which, when combined with GMDP, provided **immunostimulation** at least comparable to that from Freund's complete **adjuvant** in rabbits immunized with bovine serum albumin.

L7 ANSWER 25 OF 103 CAPLUS COPYRIGHT 2000 ACS
1994:426480 Document No. 121:26480 Effect of immunomodulators on specific tumor immunity induced by liposome-encapsulated tumor-associated antigens.
Bergers, Joep J.; Den Otter, Willem; Dullens, Hub F.J.; De Groot, Jan Willem; Steerenberg, Peter A.; Filius, P. Margreet G.; Crommelin, Daan J.A. (Utrecht Inst. Pharm. Sci., Univ. Utrecht, Utrecht, 3508 TB, Neth.). Int. J. Cancer, 56(5), 721-6 (English) 1994. CODEN: IJCNAW. ISSN: 0020-7136.

AB Reconstituted membranes consist of liposomal structures formed by removal of detergent from solubilized membrane constituents. The membrane-like configuration of reconstituted membranes makes them attractive as vehicles

for presentation of tumor-assocd. antigens and induction of immune responses. In this study the potential of immunomodulators was assessed to enhance the specific immune response induced by immunization with reconstituted membranes prepd. from SL2 lymphosarcoma cells. Reconstituted membranes contg. muramyl tripeptide phosphatidylethanolamine (MTP-PE) provided better protection against a challenge with SL2 cells than did reconstituted membranes contg. alternative immunomodulators. Local administration of interleukin 2 (IL-2) at the immunization sites further augmented the protection induced by reconstituted membranes with MTP-PE, but IL-2 was ineffective when administered with plain reconstituted membranes. Immunity elicited by the triple modality of reconstituted SL2 membranes with MTP-PE and IL-2 was specific for SL2 cells. Systemic immunity was obtained against a challenge with a 100-fold higher no. of SL2 cells than was reached after immunization with reconstituted membranes alone (105 vs. 103 SL2 cells). Macrophages isolated from the peritoneal cavity of immunized mice 5-7 days after tumor challenge expressed high in vitro cytotoxicity. However, in contrast to the obsd. specificity of the systemic immunity, the macrophages killed both SL2 cells and nonrelated P815 cells. Neither major cytotoxic lymphocyte activity nor substantial cytotoxic antibody titers were detectable. These results indicate that the approach using reconstituted membranes combined with particular immunomodulators warrants further exploration for the development of safe, well-characterized cancer vaccines.

L7 ANSWER 26 OF 103 CAPLUS COPYRIGHT 2000 ACS

1994:86197 Document No. 120:86197 Role of **adjuvants** in the modulation of antibody isotype, specificity, and induction of protection by whole blood-stage Plasmodium yoelii vaccines. ten Hagen, Timo L. M.; Sulzer, Alexander J.; Kidd, Marybeth R.; Lal, Altaf A.; Hunter, Robert L. (Dep. Pathol. Lab. Med., Emory Univ., Atlanta, GA, 30322, USA). J. Immunol., 151(12), 7077-85 (English) 1993. CODEN: JOIMA3. ISSN: 0022-1767.

AB Mice were immunized with whole killed blood stage P. yoelii parasites in 15 **adjuvant** formulations then boosted and challenged with parasitized blood. Five of six groups immunized with the Ag in oil-in-water emulsions or formulations without oil were protected. Formulations that induced protection contained saponin, pertussis, copolymer P1004, and detoxified RaLPS. In contrast, none of nine groups of animals immunized with Ag in water-in-oil emulsions were protected. Ineffective **adjuvants** included CFA and water-in-squalene emulsions with copolymer L141 plus detoxified RaLPS, dimethyldioctadecylammonium bromide, and mycobacterial cell wall skeletons. The antibody was measured by ELISA against disrupted parasites and by indirect fluorescent antibody (immunofluorescence) using intact parasites. Protection was assocd. with antibody of the IgG2a isotype detected by immunofluorescence but not with other isotypes detected by immunofluorescence or any type antibody detected by ELISA. The water-in-oil **adjuvants** induced high titers by ELISA but low titers by immunofluorescence. These results, together with Western blot analyses, suggested that **adjuvant** vehicles control the specificity of antibody and that this, in turn, is essential for induction of protective immune responses in this model.

L7 ANSWER 27 OF 103 CAPLUS COPYRIGHT 2000 ACS

1993:407130 Document No. 119:7130 Murine peritoneal macrophages activated by

the mycobacterial 65-kilodalton heat shock protein express enhanced microbicidal activity in vitro. Peetermans, Willy E.; Langermans, Jan A. M.; Van der Hulst, Marielle E. B.; Van Embden, Jan D. A.; Van Furth, Ralph
(Dep. Infect. Dis., Univ. Hosp., Leiden, 2300, Neth.). Infect. Immun., 61(3), 868-75 (English) 1993. CODEN: INFIBR. ISSN: 0019-9567.
AB After an i.p. injection of purified protein deriv., peritoneal macrophages
from mice infected with Mycobacterium bovis Bacillus Calmette-Guerin (BCG)
show an enhanced respiratory burst, inhibit the intracellular proliferation of Toxoplasma gondii, and kill Listeria monocytogenes more efficiently than peritoneal macrophages from normal mice. One of the immunodominant antigens of Mycobacterium spp. is the 65-kDa heat shock protein (Hsp 65), and in the present study, it was detd. whether injection
of this protein into mice leads to activation of their peritoneal macrophages. After an i.p. injection of Hsp 65, peritoneal macrophages from BCG-infected CBA/J mice also released more H2O2, inhibited the proliferation of T. gondii, and killed L. monocytogenes faster than peritoneal macrophages from normal mice, although Hsp 65 was less effective than purified protein deriv. When normal mice were injected with Hsp 65 suspended in saline after a booster injection with Hsp 65, their macrophages did not display enhanced antimicrobial activity, indicating that an **adjuvant** was required for a cellular immune response against Hsp 65. In the present study, the **adjuvant** di-Me dioctadecylammonium bromide (DDA) was preferred because it contains no endotoxin or mycobacterial antigens and because it has been reported that DDA does not induce the prodn. of gamma interferon. Peritoneal macrophages from C57BL/6 and CBA/J mice that had received a s.c. injection
of Hsp 65 suspended in DDA followed by an i.p. booster injection of Hsp 65
suspended in saline were activated, as indicated by the enhanced prodn. of
H2O2, inhibition of the intracellular proliferation of T. gondii, and increased rate of intracellular killing of L. monocytogenes in vitro relative to that by resident peritoneal macrophages and peritoneal macrophages obtained from mice that had received ovalbumin instead of Hsp 65. The rate of phagocytosis of L. monocytogenes was not affected by Hsp 65 treatment. Despite the in vitro expression of enhanced microbicidal activity of peritoneal macrophages, no difference in the growth of L. monocytogenes in the liver and spleen between Hsp 65-treated and control mice was found.

L7 ANSWER 28 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 5
1993:346762 Document No.: PREV199396043762. Immunoadjuvant activity of a liposomal IL-6 formulation. Duits, Ashley J. (1); Van Puijenbroek, Andre; Vermeulen, Hans; Hofhuis, Frans M. A.; Van De Winkel, Jan G. J.; Capel, Peter J. A.. (1) Dep. Immunol., Univ. Hosp. Utrecht, G04.614, PO Box 85500, 3508 GA Utrecht Netherlands Antilles. Vaccine, (1993) Vol. 11, No. 7, pp. 777-781. ISSN: 0264-410X. Language: English.
AB The **adjuvant** effect of interleukin 6 (IL-6) entrapped in liposomes was evaluated using a 65 kDa heat shock protein as a model antigen. The secondary humoral immune response either to antigen alone, or
incorporated into liposomes, and the effect of IL-6 entrapped in liposomes, on this response were studied in Balb/c mice. The adjuvanticity
of these formulations was compared with that of potent **adjuvants** such as Ribi and dimethyldioctadecylammoniumbromide (DDA). The importance

of IL-6 during **adjuvant** activity was supported by the observation that high serum IL-6 levels were induced in Balb/c mice by all members of a panel of **adjuvants** tested. Following incorporation into liposomes, IL-6 retained its full biological activity, as shown by its capacity to sustain growth of the IL-6-dependent B9 cell line. At antigen dosages where Ribi and DDA gave minimal or no secondary antibody titres, incorporation of antigen into liposomes resulted in measurable secondary antibody titres. Interestingly, this **adjuvant** activity was significantly enhanced when liposomes containing IL-6 were co-injected with the liposomal antigen formulation. These results illustrate the potential **adjuvant** properties of this formulation, which seem especially useful for vaccines containing weak or non-immunogenic antigens.

L7 ANSWER 29 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1993:520163 Document No.: PREV199396133570. Adjuvanticity of dimethyldioctadecylammonium bromide, complete Freund's **adjuvant** and Corynebacterium parvum with respect to host immune response to coccidial antigens. Lillehoj, H. S. (1); Lindblad, E. B.; Nichols, M.. (1) USDA, Agric. Res. Serv., Livestock and Poult. Sci. Inst., Protozoan Dis. Lab., Beltsville Agric. Res. Cent., Beltsville, MD 20705 USA. Avian Diseases, (1993) Vol. 37, No. 3, pp. 731-740. ISSN: 0005-2086. Language: English. Summary Language: English; Spanish.

AB Immune response of chickens to Eimeria was investigated following immunization with coccidial antigens in combination with various immunological **adjuvants**. The adjuvanticity of dimethyl dioctadecyl ammonium bromide (DDA) was comparable to that of two other **adjuvants** known to stimulate cell-mediated immunity: complete Freund's **adjuvant** (CFA) and Corynebacterium parvum. However, DDA is considered less toxic than CFA and-appeared to evoke longer-lasting immunity than C. parvum. In general, intramuscular immunization of chickens with merozoite antigens in DDA engendered higher protective immunity than did oral immunization. Immunization of chickens with merozoite antigens in CFA, DDA, or C. parvum engendered serum IgG and biliary secretory IgA (sIgA) antibody responses, as well as coccidial antigen-specific T-cell lymphoproliferation responses. This study presents evidence that DDA acts as an **adjuvant** for both coccidia antigen-specific antibody and T-cell immunity in the avian system.

L7 ANSWER 30 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 6
1994:320926 Document No. 120:320926 Comparison of dimethyl dioctadecyl ammonium bromide, Freund's complete **adjuvant** and mineral oil for induction of humoral antibodies, cellular immunity and resistance to Newcastle disease virus in chickens. Katz, David; Inbar, Itzhak; Samina, Itzhak; Peleg, Ben-Ami; Heller, Dan E. (Isr. Inst. Biol. Res., Heb. Univ., Rehovot, 70450, Israel). FEMS Immunol. Med. Microbiol., 7(4), 303-13 (English) 1993. CODEN: FIMIEV. ISSN: 0928-8244.

AB Di-Me dioctadecyl ammonium bromide (DDA), a lipophilic quaternary amine, was evaluated in adult chickens for potentiation of immunol. responses to s.c. administered inactivated Newcastle disease virus (NDV) vaccines. DDA enhanced humoral and cell-mediated immune (CMI) responses to levels which were significantly higher than those induced by the vaccine alone The hemagglutination inhibition antibody titers induced by DDA were slightly lower than those induced by mineral oil although neutralizing antibody titers seemed to be higher. DDa induced strong CMI (DTH and lymphocyte

proliferation) responses, more than those induced by Freund's complete **adjuvant** and mineral oil. Both DDA and mineral oil induced comparable high levels of protection to challenge doses of 200000 LD50 per chicken. No toxic effects or local tissue damage were obsd. in any of the inoculated chickens.

L7 ANSWER 31 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 7
1992:610240 Document No. 117:210240 DDA as an immunological **adjuvant**. Hilgers, L. A. T.; Snippe, H. (Cent. Lab., Solvay S.A., Brussels, B-1120, Belg.). Res. Immunol., 143(5), 494-503 (English) 1992. CODEN: RIMME5. ISSN: 0923-2494.
AB A review with 83 refs. As compared to other **adjuvants**, dimethyldioctadecylammonium bromide (DDA) is a moderate or strong **adjuvant** for humoral responses and a strong **adjuvant** for cell-mediated immunity, esp. delayed hypersensitivity responses, against different types of antigens and in both lab. animals and larger animals. DDA can collaborate with other immunomodulating compds. resulting in further enhanced responses. This **adjuvant** can be applied in exptl. vaccines and in com. vaccines for veterinary purposes. In immunol., DDA can be uf use to study T helper cells responsible for delayed hypersensitivity responses and to characterize T helper cell epitopes on antigens.

L7 ANSWER 32 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
92246600 EMBASE Document No.: 1992246600. Characteristics and practical use of new-generation **adjuvants** as an acceptable alternative to Freund's complete **adjuvant**: Introduction. Claassen E.; Boersma W.J.A.. Dept. Immunology/Med. Microbiology, Medical Biological Laboratory, Dutch Organisation Applied Sci. Res., POB 45,2280 AA Rijswijk, Netherlands. Research in Immunology 143/5 (475-477) 1992. ISSN: 0923-2494. CODEN: RIMME5. Pub. Country: France. Language: English.

L7 ANSWER 33 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 8
1992:119250 Document No.: BA93:65050. **ADJUVANT** EFFECTS OF DIMETHYL DIOCTADECYL AMMONIUM BROMIDE COMPLETE FREUND'S **ADJUVANT** AND ALUMINIUM HYDROXIDE ON NEUTRALIZING ANTIBODY ANTIBODY-ISOTYPE AND DELAYED-TYPE HYPERSENSITIVITY RESPONSES TO SEMLIKI FOREST VIRUS IN MICE. KATZ D; LEHRER S; GALAN O; BAR-EL LACMI; COHEN S. DEP. VIROLOGY, ISRAEL INST. BIOLOGICAL RESEARCH, P.O. BOX 19, NESS-ZIONA, 70450, ISRAEL.. FEMS (FED EUR MICROBIOL SOC) MICROBIOL IMMUNOL, (1991) 76 (6), 305-320. CODEN: FMIMEH. Language: English.
AB Outbred mice were inoculated subcutaneously with inactivated Semliki Forest virus (SFV) in saline and combinations of the virus with complete Freund's **adjuvant** (CFA) aluminium hydroxide (Al) and dimethyl dioctadecyl ammonium bromide (DDA). The immune response was evaluated for delayed-type hypersensitivity, for total ELISA antibodies and antibody-isotypes and for neutralizing antibodies. DDA was the most efficient **adjuvant** in inducing DTH, CFA the second and Al induced a DTH response that was only slightly higher (statistically not significant) than that induced by the inactivated virus without **adjuvants**. All **adjuvants** enhanced the production of ELISA antibodies to similar levels. However, the levels of neutralizing antibodies induced were low in mice which were inoculated with the inactivated SFV alone or mixtures of the virus with Al. DDA induced high levels of neutralizing antibodies and CFA induced intermediate levels. The pattern of antibody-isotypes induced by DDA and CFA was different from the

pattern induced by the inactivated virus or by the virus mixed with Al: DDA and CFA induced low amounts of IgG1 antibodies and relatively higher amounts of IgG2a and IgG2b antibodies while the inactivated virus and the mixture of the virus with Al induced higher proportions of IgG1 antibodies. In sera from convalescent mice the majority of antibody activity resided in the IgG2a and IgG2b immunoglobulin subclasses, while IgG1 antibodies were undetectable.

L7 ANSWER 34 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
91248908 EMBASE Document No.: 1991248908. The effects of **adjuvants** on immune responses in cattle injected with a Brucella abortus soluble antigen. Dzata G.K.; Confer A.W.; Wyckoff III J.H.. Department of Veterinary Pathology, College of Veterinary Medicine, Oklahoma State University, Stillwater, OK 74078, United States. Veterinary Microbiology 29/1 (27-48) 1991.
ISSN: 0378-1135. CODEN: VMICDQ. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB Five different **adjuvants** were examined for potentiation of humoral and cell-mediated immune (CMI) responses in cattle to a Brucella abortus soluble antigen (BASA). Two separate experiments were performed involving a total of 64 steers, divided among six groups (Experiment 1) and 9 groups (Experiment 2). The **adjuvants** used were: muramyl dipeptide, Freund's incomplete **adjuvant**, dimethyl-dioctadecyl ammonium bromide (DDA), Bordetella pertussis and Propionibacterium acnes. In each experiment, three groups received BASA (2 mg protein) subcutaneously with **adjuvant**, one group received a reduced dose of B. abortus Strain 19 (S19), one group served as unvaccinated controls, and another group received BASA alone. Primary responses were studied following a single immunization in comparison to the single inoculation with S19. For each experiment serum antibody responses and CMI responses were sequentially determined over a period of 56 days. Antibody responses to B. abortus were measured using the brucellosis card, rivanol precipitation-plate agglutination, complement fixation, and fluorometric immunoassay tests, and as well as with an enzyme-linked immunosorbent assay. The CMI response was measured using antigen-specific lymphoproliferation (LP) and skin testing for delayed-type hypersensitivity (DTH) to BASA (Experiment 2). Specific aspects of induced CMI responses investigated were macrophage activation (IL-1 production), helper T cell activation (IL-2 production), and release of soluble suppressor factor(s). In general, mean antibody responses were significantly higher ($P < 0.05$) in immunized steers than in control steers and those receiving BASA alone. The LP responses to heat-killed B. abortus were generally higher in immunized groups than in the controls. The LP and DTH responses were greatest in the groups receiving S19 and BASA + DDA. Increased induction of IL-1 was largest in the group receiving BASA + DDA whereas IL-2 release was greatest in S19 vaccinated steers. Suppressor T cell responses were most obvious in the groups receiving S19, BASA + B. pertussis, and P. acnes. These studies demonstrated that DDA potentiates CMI responses to a soluble B. abortus antigen and may be useful as an **adjuvant** for future vaccines, particularly subunit vaccines.

L7 ANSWER 35 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 9
1992:120565 Document No. 116:120565 Immunopotentiation of cattle vaccinated with a soluble Brucella abortus antigen with low LPS content: an analysis of cellular and humoral immune responses. Dzata, G. K.; Wyckoff, John H.,

III; Confer, A. W. (Coll. Vet. Med., Oklahoma State Univ., Stillwater, OK,
74078, USA). Vet. Microbiol., 29(1), 15-26 (English) 1991. CODEN: VMICDQ. ISSN: 0378-1135.

AB The **adjuvant** effects of di-Me dioctadecyl ammonium bromide (DDA) alone or in combination with trehalose dimycolate (TDM) or muramyl dipeptide (MDP) on bovine humoral and cellular responses to a sol. protein ext. of gamma irradiated Brucella abortus strain 19 (SPEBA) were investigated. Thirty-five beef steers were randomly allotted to nine groups. Three of these groups received SPEBA (2 mg protein per dose) s.c. in combination with **adjuvants**, one group received the reduced dose of B. abortus strain 19 (S19), and one group received SPEBA alone. Controls included groups receiving **adjuvant** prepns. only or no vaccine. Immune responses to the various immunizations were assessed sequentially for 56 days using various in vitro and in vivo assays. Minimal humoral responses were induced with SPEBA alone. The highest and most sustained serum antibody responses to B. abortus antigens were elicited by the S19 vaccine. A combination of SPEBA with DDA + TDM induced higher antibody levels than SPEBA with DDA or SPEBA with DDA + MDP. Delayed hypersensitivity responses among the groups receiving SPEBA were most notable in the SPEBA with DDA + TDM groups. Increased interleukin 2 prodn. was greatest in the S19 and SPEBA with DDA + TDM vaccinates. The results indicated that a combination of DDA + TDM best potentiated immune responses to a sol. B. abortus antigen prepn. and may be useful as **adjuvants** for future vaccines.

L7 ANSWER 36 OF 103 CAPLUS COPYRIGHT 2000 ACS

1991:55892 Document No. 114:55892 Active immunization of beef heifers against luteinizing hormone: I. Evaluation of protein carriers and **adjuvants** on antigenicity of LH. Roberts, A. J.; DeAvila, D. M.; Gerber, J. D.; Reeves, J. J. (Dep. Anim. Sci., Washington State Univ., Pullman, WA, 99164-6332, USA). J. Anim. Sci., 68(11), 3742-6 (English) 1990. CODEN: JANSAG. ISSN: 0021-8812.

AB Two expts. were conducted to evaluate two carrier proteins and nine **adjuvants** in promoting antibody prodn. in heifers immunized against LH. The anti-LH antibody response was evaluated in heifers immunized against LH conjugated to either ovalbumin or keyhole limpet hemocyanin (KLH) (Exp. 1). In Exp. 2, an LH-ovalbumin conjugate was used to evaluate effectiveness of nine different **adjuvants** in antibody prodn. Weekly blood samples were collected from all heifers throughout the 23-wk study to det. LH antibody binding activity. Exp. 1, heifers immunized with the LH-ovalbumin (LH-oval) conjugate had greater LH antibody binding activities than those immunized with the LH-KLH conjugate. In Exp. 2, nine groups of heifers were immunized with LH-oval suspended in one of nine **adjuvants**; a 10th group was immunized against ovalbumin alone (control). Only **adjuvants** that contained at least 40% oil resulted in LH antibody binding activity that differed from control. These results show that ovalbumin was a superior carrier protein to KLH in enhancing antibody prodn.; **adjuvants** with greater than 50% oil were superior to those with less oil in promoting LH antibody prodn.

L7 ANSWER 37 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

90219749 EMBASE Document No.: 1990219749. Synthetic immunomodulating agents. Georgiev V.S.. Division of Life Sciences, Orion Research and Technologies Corp., P.O. Box 463, Tampa, FL 33601-0463, United States. Medicinal Research Reviews 10/3 (371-409) 1990.
ISSN: 0198-6325. CODEN: MRREDD. Pub. Country: United States. Language:

English.

L7 ANSWER 38 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 10
1990:589380 Document No. 113:189380 The effect of **adjuvants** on antibody titers in mouse vaginal fluid after intravaginal immunization. Thapar, Manjula A.; Parr, Earl L.; Parr, Margaret B. (Sch. Med., South. Illinois Univ., Carbondale, IL, 62901, USA). J. Reprod. Immunol., 17(3), 207-16 (English) 1990. CODEN: JRIMDR. ISSN: 0165-0378.
AB Intravaginal (ivag) immunization elicits secretory immune responses in the female reproductive tract, but little is known about the safety and effectiveness of **adjuvants** for such immunization. Mice were immunized intravaginally once daily for 5 days with large doses of horse ferritin combined with aluminum hydroxide (AH), muramyl dipeptide (MDP), monophosphoryl lipid A (MPL), di-Me dioctadecyl ammonium bromide (DDA), or cholera toxin (CT). Titers of anti-ferritin IgA and IgG were measured in vaginal fluid by ELISA. The most effective **adjuvant** for ivag primary immunization was AH, while MPL was most effective for ivag boosting. None of the **adjuvants** caused a detectable tissue reaction in vaginal mucosa. Primary ivag immunization for 5 days with ferritin and AH followed by ivag boosting for 5 days with ferritin and MPL elicited higher IgA titers in vaginal fluid than systemic priming and boosting with ferritin and AH or systemic priming and ivag boosting with ferritin and MPL. Systemically immunized animals exhibited the highest IgG titers in vaginal fluid. Thus, **adjuvants**, particularly AH, can increase local immune responses to intravaginal immunization, but it should be noted that multiple applications of large doses of antigen were used and that this route of sensitization may be relatively inefficient.

L7 ANSWER 39 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
90274726 EMBASE Document No.: 1990274726. [Application of immunomodulators against infectious diseases]. DER EINSATZ VON IMMUNOMODULATOREN BEI INFEKTIONSKRANKHEITEN. Masihi K.N.; Rohde-Schulz B.. Robert Koch-Institut des Bundesgesundheitsamtes, Nordufer 20, D-1000 Berlin 65, Germany. Arztliche Laboratorium 36/8 (207-212) 1990.
ISSN: 0001-9526. CODEN: AELAAH. Pub. Country: Germany. Language: German. Summary Language: English.
AB Despite major advances in the field of active immunization the global incidence of infectious diseases continues unabated. The development of new potent vaccines with high adjuvanticity and the concept of enhancing the host's nonspecific defense mechanisms are important aspects in the immunoprophylaxis and therapy of infectious diseases. A number of immunomodulating substances are able to induce effective nonspecific resistance to a wide spectrum of viral, bacterial and parasitic infections in vivo and possess potent **adjuvant** activity.

L7 ANSWER 40 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 11
1990:83924 Document No. 112:83924 Immunization of cattle against modified peptides of gonadotropin releasing hormone conjugated to carriers: effectiveness of Freund's and alternative **adjuvants**. Goubau, S.; Silversides, D. W.; Gonzalez, A.; Laarveld, B.; Mapletoft, R. J.; Murphy, B. D. (Dep. Anim. Poult. Sci., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.). Theriogenology, 32(4), 557-67 (English) 1989. CODEN: THGNBO. ISSN: 0093-691X.
AB Two gonadotropin-releasing hormone (GnRH) peptides with a cysteine substitution of the first (C1-CnRH) or tenth (C10-GnRH) amino acid were conjugated to ovalbumin and equine serum albumin, resp., via the sulfhydryl group of the introduced cysteine. Animals were immunized three

times at 3-wk intervals with both conjugates in either saline, Freund's complete **adjuvant** (FCA), Havlogen, Ribi **adjuvant** system (RAS), dimethyldioctadecylammonium bromide (DDA), Alhydrogel, or Regressin. Animals immunized with conjugates in saline or RAS did not produce anti-GnRH titers. The highest anti-GnRH titers were produced by animals treated with FCA. The Alhydrogel and DDA treatments stimulated the prodn. of GnRH antibodies in all animals treated, but titers were lower than in aminals immunized with FCA. When vaccines were formulated with Havlogen or Regressin, anti-GnRH titers were low or absent. Serum LH and FSH levels were depressed in FCA and in Alhydrogel treated animals. The antisera raised were predominantly directed against either the carboxy- or the amino-terminal end of the GnRH peptide, or directed equally against both, depending on the individual animal. Results suggest that no epitope of GnRH dominates the immune response in cattle and show that the best alternative to FCA is Alhydrogel.

L7 ANSWER 41 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 12
1990:30378 Document No. 112:30378 Synergistic effects of locally administered cytostatic drugs and a surfactant on the development of delayed-type hypersensitivity to keyhole limpet hemocyanin in mice. Limpens, J.; Scheper, R. J. (Dep. Pathol., Free Univ. Hosp., Amsterdam, Neth.). Clin. Exp. Immunol., 78(2), 256-62 (English) 1989. CODEN: CEXIAL. ISSN: 0009-9104.

AB The immunomodulating effects of two locally administered cytostatic drugs, the active cyclophosphamide deriv. Z 7557 and the plant alkaloid VP-16, were compared with the effects of systemically administered cyclophosphamide and several established **adjuvants**: Freund's complete **adjuvant**, dextran sulfate, and di-Me dioctadecyl ammonium bromide (DDA). All agents tested promoted the development of delayed-type hypersensitivity (DTH) to keyhole limpet hemocyanin (KLH) in mice. Locally administered cytostatic drugs were the most effective **immunostimulatory** compds., whereas DDA was the least toxic agent tested. In order to increase the effectiveness and/or reduce the toxicity of these agents the authors tested the efficacy of combinations of cytostatic drugs and DDA to enhance DTH. The results show that DDA and suboptimal amts. of locally administered cytostatic drugs act synergistically on DTH.

L7 ANSWER 42 OF 103 CAPLUS COPYRIGHT 2000 ACS
1989:449926 Document No. 111:49926 **Adjuvant** activity of water-insoluble surfactants. Woodard, Lynn F. (USA). Lab. Anim. Sci., 39(3), 222-5 (English) 1989. CODEN: LBASAE. ISSN: 0023-6764.

AB A series of cationic amine and diamine surfactants, nonionic surfactants, and traditional vaccine **adjuvants** were compared for capacity to induce serum IgG antibody. With one exception, none of the aliph. primary, secondary, tertiary, or quaternary amines or diamines exhibited **adjuvant** activity beyond that of the dil. hexadecane emulsion vehicle nor was a structure-activity relationship detd. Avridine, a lipoidal diamine, potentiated the antibody response, but not to the level of some nonionic surfactant **adjuvants** or Freund's **adjuvants**. Among the nonionic surfactants, T1501 tetronic block copolymer, trehalose dimycolate, sorbitan trioleate, and glycerol trioleate were equiv. to Freund's complete **adjuvant** in their capacity to stimulate antibody. The latter 2 surfactants have not been reported previously. Thus, certain nonionic surfactants in dil. oil-in-water emulsions are effective replacements for Freund's **adjuvants**. Such **adjuvant** emulsions are easily prepd.,

easily injected and do not produce the grossly adverse reaction obsd. with
Freund-type water-in-oil emulsions.

L7 ANSWER 43 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
89256006 EMBASE Document No.: 1989256006. Comparison of protective immunity and inflammatory responses of pigs following immunization with different Actinobacillus pleuropneumoniae preparations with and witout **adjuvants**. Hall W.; Molitor T.W.; Joo H.S.; Pijoan C.. Department of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Minnesota, St. Paul, MN 55108, United States. Veterinary Immunology and Immunopathology 22/2 (175-186) 1989.
ISSN: 0165-2427. CODEN: VIIMDS. Pub. Country: Netherlands. Language: English. Summary Language: English.
AB Three experiments were performed to evaluate the inflammatory response, the antibody response and protection from experimental challenge of various Actinobacillus pleuropneumoniae serotype 5 (Ap5) vaccines in swine. In the first experiment, subcutaneous injections of either a water-in-oil (W/O) emulsion or Freund's complete **adjuvant** (FCA) caused lesions at the site of injection, while intraperitoneal injection of the W/O emulsion caused no lesions. In the second experiment, intraperitoneal (IP) injection of a W/O emulsion containing unwashed Ap5 cells (6-h culture) and/or supernates from a 24-h culture resulted in severe peritoneal lesions, while W/O emulsion containing PBS-washed Ap5 cells resulted in minimal peritoneal lesions. Ap5 alone or W/O alone failed to cause peritoneal lesions. The third experiment compared the antibody response to protection from challenge of pigs immunized with either 6-h PBS-washed Ap5 cells emulsified in oil - IP, 6-hour Ap5 cells adjuvanted with dimethyl diodacyl ammonium bromide - IP, Ap5 antigen alone
- IP, a commercial vaccine - subcutaneously or saline - IP. All groups, except the saline-treated group, responded with high antibody titers to Ap5 2 weeks following vaccination; however, titers from the W/O plus antigen group were significantly higher than the three other groups ($P < 0.05$). Following intranasal challenge with Ap5, all animals responded with
increased antibody titers. All pigs were euthanized 10 days after challenge and evaluated for pneumonia and the lungs cultured for bacteria.
The lungs of all pigs, excepting the W/O plus antigen group, contained pneumonic lesions and A. pleuropneumoniae was cultured from these lesions.
These results, along with results from other groups, suggest that intraperitoneal immunization using oil-adjuvanted vaccine may be an effective method for protecting pigs from pneumonia deu to A. pleuropneumoniae. Its efficacy may be due to stimulation of local respiratory mucosal immunity.

L7 ANSWER 44 OF 103 CAPLUS COPYRIGHT 2000 ACS
1990:623915 Document No. 113:223915 The immunoadjuvant dimethyldioctadecylammonium bromide. Snippe, H.; Kraaijeveld, C. A. (Fac. Med., Utrecht Univ., Utrecht, Neth.). NATO ASI Ser., Ser. A, 179(Immunol. Adjuvants Vaccines), 47-59 (English) 1989. CODEN: NALSDJ.
AB A review with .apprx.75 refs. The title **adjuvant** stimulates esp. cell-mediated immunity and has a no. of advantages over other clin. applied **adjuvants**.

L7 ANSWER 45 OF 103 CAPLUS COPYRIGHT 2000 ACS
1988:516078 Document No. 109:116078 Stabilized **adjuvant** suspension

for vaccines, comprising dimethyl dioctadecyl ammonium bromide. Hilgers, Lucas Alfonsus Theodorus; Weststrate, Marinus Wijnand (Duphar International Research B. V., Neth.). Eur. Pat. Appl. EP 273512 A2 19880706, 2 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1987-202523 19871215. PRIORITY: NL 1986-3232 19861219.

AB The title suspensions of Me2(C18H37)2NBr (DDA) are stabilized by water-sol. acrylic acid polymers. Suspensions comprising .gtoreq.1 wt. part Carbopol per part DDA contain a small amt. of ppt. after 2 mo incubation at 37.degree.; the ppt. is readily resuspended by shaking. Carbopol-stabilized suspensions resist pptn. after 20 min autoclaving at 127.degree. and after centrifuging for 30 min at 5000 rpm (3000g).

L7 ANSWER 46 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 13

1989:127909 Document No. 110:127909 Serum amyloid P component induction by immunomodulators. Hilgers, L. A. T.; De Reuver, M. J.; Vaandrager, A. R.; Ong, T.; Snippe, H.; Willers, J. M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, NL-3511GG, Neth.). Nat. Immun. Cell Growth Regul., 7(5-6), 328-35 (English) 1988. CODEN: NICRDR. ISSN: 0254-7600.

AB The capacity of immunoadjuvants to enhance serum amyloid P component (SAP) levels and to modulate the humoral immune response to sheep red blood cells in a no. of different mouse strains was investigated. Although the synthetic **adjuvants** dimethyldioctadecylammonium bromide, dextran sulfate and bacterial-derived lipopolysaccharide did not enhance SAP levels in some of the mouse strains tested, these strains responded normally to the immunomodulating effects of the **adjuvants**. It is concluded that increased SAP levels and modulation of immune responses are induced via at least partially different pathways. For these reasons, it is impossible to screen drugs for potential **adjuvant** activity by only measuring SAP levels in mice.

L7 ANSWER 47 OF 103 CAPLUS COPYRIGHT 2000 ACS

1989:133446 Document No. 110:133446 Purified glycoproteins of influenza virus stimulate cell-mediated cytotoxicity in vivo. Arora, D. Jit S.; Houde, Michel (Inst. Armand-Frappier, Univ. Quebec, Laval-des-Rapides, PQ, H7N 4Z3, Can.). Nat. Immun. Cell Growth Regul., 7(5-6), 287-96 (English) 1988. CODEN: NICRDR. ISSN: 0254-7600.

AB Previously, the authors reported that purified surface influenza viral glycoproteins can induce cell-mediated cytotoxicity (CMC) in vitro. Both neuraminidase (NA) and hemagglutinin (HA) were equally good stimulators, on an equimolar basis. Here, it was examd. whether these glycoproteins stimulate natural killer (NK) activity in vivo. Biol. active prepns. of glycoproteins NA and HA were purified from virus A/USSR/90/77 (H1N1) and recombinant virus A/USSR/92/77 (H1) .times. A/Prague/1/56 (N7), resp. In a 4-h NK assay, using NK-sensitive YAC-1 cells as targets, both viral glycoproteins stimulated the NK activity of splenocytes of BALB/c and C3H mice. This stimulation was independent of the route of administration (i.v. or i.p.) of the antigen. The obsd. NK activity was viral antigen-specific and could be modulated to levels comparable to those obsd. with the std. stimulator, polyinosinic acid-polycytidylic acid, by the use of an appropriate synthetic **adjuvant**, stearyl tyrosinate. The evidence suggests that the enhanced CMC is due to NK cells. These observations imply that enhancement of NK activity is the intrinsic property of influenza NA and HA.

L7 ANSWER 48 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 14

1988:596972 Document No. 109:196972 Preparation and characterization of

liposomes with incorporated Neisseria gonorrhoeae protein IB and amphiphilic **adjuvants**. Van Dalen, Frans; Kersten, Gideon; Teerlink, Tom; Beuvery, E. Coen; Crommelin, Daan J. A. (Dep. Pharm., Univ. Utrecht, Utrecht, 3522 AD, Neth.). J. Controlled Release, 7(2), 123-32 (English) 1988. CODEN: JCREEC. ISSN: 0168-3659.

AB Liposomes were prepd. according to a 3-step procedure. Octyl glucoside, lipid and optionally protein (outer membrane protein IB from N. gonorrhoeae), lipid A or dimethyldioctadecylammonium bromide (DDA) contg. mixed micelle dispersions were dild., then dialyzed and finally filtered. The liposome prepns. were characterized for their particle size (both freshly prepd. and after storage) and the contents of the different constituents. Data on the orientation of protein IB in the bilayer were collected. Stable, well-defined liposomes could be obtained with egg phosphatidylcholine/cholesterol bilayers contg. optionally DDA or lipid A with or without protein IB. For dipalmitoylphosphatidylcholine/cholesterol combinations a charge-inducing agent [DDA or dipalmitoylphosphatidylglycerol (DPPG)] was required to stabilize the liposomes which further contained (optionally) lipid A (only with dipalmitoylphosphatidylcholine/cholesterol/DPPG) with or without protein IB. In general, the uptake of all constituents into the bilayer was almost quant. Enzymic degrdn. expts. showed that protein IB had the same orientation and surface exposure as in the bacteria outer membrane.

L7 ANSWER 49 OF 103 CAPLUS COPYRIGHT 2000 ACS

1989:121166 Document No. 110:121166 A synthetic luteinizing hormone releasing hormone vaccine II. Temporal aspects of titer development and formulation trials in BALB/c mice. Silversides, D. W.; Allen, A. F.; Misra, V.; Murphy, B. D.; Mapletoft, R. J. (Dep. Vet. Physiol., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.). J. Reprod. Immunol., 14(1), 47-58 (English) 1988. CODEN: JRIMDR. ISSN: 0165-0378.

AB Cysteine-substituted analogs of LH-releasing hormone (LHRH) were coupled to carrier mols., and the resulting conjugates used to characterize the immune response to native LHRH generated in BALB/c mice and to formulate vaccines in an effort to maximize titer development. In an active immunization trial designed to characterize temporal aspects of anti-LHRH titer development, titers could be detected 1 wk after initial immunization. No differences were obsd. in response between male and female mice. Booster immunizations could enhance the titers against LHRH. Then titers developed against the carrier mol. were uniformly higher than the corresponding anti-LHRH titers throughout the course of the trial. In sep. trials, vaccines were formulated and tested in BALB/c mice for titer development against LHRH. **Adjuvants**, carrier mols. dosage and peptide to carrier ratio were considered. Dosages of 50 .mu.g conjugate per immunization per mouse, at conjugation ratios of 3-12 peptides per 105 Dalton carrier mol., produced immune responses. **Adjuvants** including Havlogen and dimethyldioctadecylammonium bromide, and carrier mols. including keyhole limpet hemocyanin, porcine thyroglobulin and equine .gamma.-globulin were all effective.

L7 ANSWER 50 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS

1988:327157 Document No.: BR35:32491. INFLUENCE OF PHYSICAL PRESENTATION FORM OF GONOCOCCAL OUTER MEMBRANE PROTEIN IB ON THE HUMORAL IMMUNE RESPONSE. TEERLINK T; KERSTEN G F A; JISKOOT W; PAQUES M; CROMMELIN D J A; BEUVERY E C. DEP. BACTERIAL VACCINES AND INACTIVATED VIRAL VACCINES, NATL. INST. FOR

PUBLIC HEALTH AND ENVIRONMENTAL HYGIENE RIVM , P.O. BOX 1, 3720 BA BILTHOVEN, NETHERLANDS.. SYMPOSIUM ON TECHNOLOGICAL ADVANCES IN VACCINE DEVELOPMENT HELD AT THE 17TH ANNUAL UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, PARK CITY, UTAH, USA, JANUARY 30-FEBRUARY 6, 1988. J CELL BIOCHEM SUPPL. (1988) 0 (12 PART B), 11. CODEN: JCBSD7. Language: English.

L7 ANSWER 51 OF 103 CAPLUS COPYRIGHT 2000 ACS

1987:194221 Document No. 106:194221 In vitro proliferation of lymphocytes from cyclophosphamide-pretreated mice immunized with antigen mixed with dimethyl dioctadecyl ammonium bromide. Ziola, Barry; Smith, Richard H.; Qualtiere, Louis F. (Dep. Microbiol., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.). J. Immunol. Methods, 97(2), 159-64 (English) 1987. CODEN: JIMMBG. ISSN: 0022-1759.

AB A blastogenesis assay employing lymphocytes from cyclophosphamide-pretreated mice immunized with antigen mixed with the immunopotentiating compd. di-Me dioctadecyl ammonium bromide is described. The model antigen used for detg. the assay parameters was inactivated purified measles virus. The optimal time for removal of immunol. primed T cells was 7 days after immunization of mice pretreated 2 days previously with 200mg of cyclophosphamide/kg. The peak lymphoproliferative response occurred after 3-5 days in culture, depending on the concn. of antigen used. Although fetal bovine serum and syngeneic mouse serum each worked well as a medium supplement, significantly higher specific and lower non-specific lymphoproliferation were obtained when the mouse serum was used. Most of the lymphocytes responding to antigen were of the Ly 1.2 phenotype. Specificity of the blastogenic response was shown by a lack of cross-reactivity among measles virus, herpes simplex virus type 1 and vesicular stomatitis virus antigens. This approach to a mouse blastogenesis assay involves an easy way to induce strong T cell priming in mice, while still providing an assay which has an ideal combination of low non-specific and high antigen-specific responses.

L7 ANSWER 52 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 15

1986:532024 Document No. 105:132024 T-cell-independent macrophage activation in mice induced with rRNA from Listeria monocytogenes and dimethyldioctadecylammonium bromide. Van den Bosch, Johannes F.; Kanis, Iris Y. R.; Antonissen, Ad C. J. M.; Buurman, Wim A.; Van Boven, Cees P. A. (Dep. Med. Microbiol., Univ. Limburg, Maastricht, 6200 MD, Neth.). Infect. Immun., 53(3), 611-15 (English) 1986. CODEN: INFIBR. ISSN: 0019-9567.

AB Purified rRNA from L. monocytogenes or Pseudomonas aeruginosa injected in combination with dimethyldioctadecylammonium bromide (DDA), protects mice nonspecifically against a lethal challenge of various extra- and intracellular bacteria. In the present study vaccination of BALB/c as well as C57BL/Ka mice with listerial RNA-DDA resulted in activation of fixed-tissue macrophages, as measured by an enhanced in vivo L. monocytogenes killing in spleen and liver. Macrophage activation by vaccination with rRNA-DDA occurred by a T-cell-independent mechanism. Treatment of mice with cyclosporin A had no effect on the enhanced L. monocytogenes killing induced with RNA-DDA; in vitro exposure of RNA-DDA to spleen cell cultures did not give rise to any lymphocyte proliferation.

No evidence could be found for a possible **adjuvant** activity for RNA-DDA in cellular responses; in fact, RNA-DDA had an inhibitory effect on lymphocyte proliferative responses to Listeria antigen and to Con A.

L7 ANSWER 53 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 16
1986:199758 Document No. 104:199758 Synergistic effects of synthetic **adjuvants** on the humoral immune response. Hilgers, L. A. T.; Snippe, H.; Jansze, M.; Willers, J. M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, NL-3511 GG, Neth.). Int. Arch. Allergy Appl. Immunol., 79(4), 392-6 (English) 1986. CODEN: IAAAAM. ISSN: 0020-5915.

AB The effect of combinations of **adjuvants** on the humoral immune response to sheep red blood cells (SRBC) as antigen was investigated. **Adjuvants** belonging to 2 categories differing in physicochem. properties were used: surfactants (N,N-dioctadecyl-N',N'-bis(2-hydroxyethyl)propanediamine (CP-20961) [35607-20-6], dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**], neutrally charged liposomes, polyol (polyol L 101 [9003-11-6] and polyol L 121 [9003-11-6]) and polyanions [dextran sulfate (DXS) [9042-14-2], liquoid [9056-83-1], and suramine [145-63-1]]. All **adjuvants** but suramine augmented humoral responses to 2 .times. 107 SRBC measured by the no. of direct anti-SRBC plaque-forming cells (PFC) in the spleen. The response to 2 .times. 106 SRBC was enhanced considerably by L 121 and DXS but hardly or not at all by the other **adjuvants**. Combinations of 2 **adjuvants** were made at distinct ratios (1:3, 2:2, and 3:1) and injected i.p. with 2 .times. 106 SRBC. Low responses (5 .times. 103 PFC per spleen) were induced by combinations of liquoid or suramine with DDA or DXS, and by combinations of CP-20961, liposomes, L 101 or L 121 with DDA. Combinations of the surfactants DDA, CP-20961, liposomes, L 101 or L 121 with DXS evoked responses which were significantly higher than the sum of responses supported by the single **adjuvants**. Ratios of 1:3 or 2:2 (surfactant:DXS) resulted in the most effective combinations. The data suggest that only **adjuvants** derived from 2 different physicochem. groups are able to act synergistically.

L7 ANSWER 54 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 17
1986:102156 Document No. 104:102156 Route-dependent immunomodulation: local stimulation by a surfactant and systemic stimulation by a polyanion. Hilgers, L. A. T.; Snippe, H.; Jansze, M.; Willers, J. M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, NL-3511 GG, Neth.). Int. Arch. Allergy Appl. Immunol., 79(4), 388-91 (English) 1986. CODEN: IAAAAM. ISSN: 0020-5915.

AB Immunomodulatory activity of the 2 synthetic **adjuvants** dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**] and dextran sulfate (DXS) [9042-14-2] in relation to route and time of injection was investigated in mice. Humoral responses to sheep red blood cells (SRBC) were measured as the no. of direct anti-SRBC plaque-forming cells (PFC) in the spleen 5 days after immunization. Both **adjuvants** stimulated the anti-SRBC response if **adjuvant** and antigen were injected simultaneously via the same route (either i.p. or i.v.). Administration of **adjuvant** and antigen via different routes (i.p. or i.v., resp. or vice versa) resulted in enhanced humoral responses after DXS but not after DDA. I.p. immunization of mice which were injected i.p. with either **adjuvant** 4 days earlier resulted in diminished humoral responses. Immune reponses in pretreated mice were not suppressed when the antigen was injected i.v. instead of i.p. In conclusion, DDA and DXS differ in immnostimulating properties as DDA enhanced only a response to antigen injected via the same route whereas DXS induced a systemic state of increased immunoresponsiveness. The immunosuppressive state induced by i.p. injection of either **adjuvant** prior to immunization is restricted to the peritoneal

compartment. Mechanisms underlying differences between both **adjuvants** and aspects of systemic immunopotentiation are discussed.

L7 ANSWER 55 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 18
1987:38310 Document No. 106:38310 Immunogenic activity of gonococcal protein
I in mice with three different lipoidal **adjuvants** delivered in liposomes and in complexes. Jiskoot, Wim; Teerlink, Tom; Van Hoof, Monique M. M.; Bartels, Kees; Kanhai, Vishna; Crommelin, Daan J. A.; Coen Beuvery, E. (Dep. Pharm., State Univ. Utrecht, Utrecht, 3511 GH, Neth.). Infect. Immun., 54(2), 333-8 (English) 1986. CODEN: INFIBR. ISSN: 0019-9567.

AB For several reasons the major outer membrane protein from Neisseria gonorrhoeae (gonococcal protein [PI]) is an attractive component for a gonococcal vaccine. The effect of 2 different phys. forms of PI on its immunogenic activity was studied. PI was delivered in liposomes and in protein-detergent complexes. In both forms PI was present in a multimeric form. The liposomes were composed of phosphatidylcholine and cholesterol.
The effect of dicetyl phosphate [2197-63-9] as a neg. charged amphiphile and 3 lipoidal **adjuvants** was investigated. Two lipoidal **adjuvants** (Avridine [35607-20-6] and dimethyldioctadecylammonium bromide [**3700-67-2**]) were pos. charged amphiphiles, whereas the 3rd one (tridecyl N-acetylmuramyl-L-alanyl-D-isoglutaminate [106022-53-1]) was neutral. The protein-detergent complexes were also tested in the presence of the lipoidal **adjuvants** and in an AlPO4-adsorbed form. The liposome reparations were characterized for their size, charge, and residual amt. of detergent. The immunogenic activity of PI in all forms was tested in mice. The results of the antibody assays showed that PI in the liposomes was more immunogenic than PI in the complexes. A second dose with liposomes induced only a small booster effect, whereas such a dose with the complexes produced pronounced booster effects. The incorporation of the pos. charged lipoidal **adjuvants** in the liposomes resulted in enhanced booster effects. The highest immunogenic activity of PI after 2 injections, however, was obsd. in the complexed form adsorbed to AlPO4.

L7 ANSWER 56 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 19
1986:404737 Document No. 105:4737 Suppression of the cellular adjuvanticity of lipophilic amines by a polyanion. Hilgers, Luuk A. T.; Snippe, Harm; Van Vliet, Karin E.; Jansze, Margriet; Willers, Jan M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, Neth.). Int. Arch. Allergy Appl. Immunol., 80(3), 320-5 (English) 1986. CODEN: IAAAAM. ISSN: 0020-5915.

AB Modulation of delayed-type hypersensitivity reaction (DTH) in mice by synthetic **adjuvants** and the mode of their action were investigated. Intracutaneous injection of azobenzenearsonate coupled to phosphatidylethanolamine (A-PE) without **adjuvant** did not induce DTH. Administration of A-PE with the quaternary amines dimethyldiocatadecylammonium bromide (DDA) or N,N-dioctadecyl-N',N'-bis(2-hydroxyethyl)propane diamine (CP-20,961) induced a strong response. Other surfactants, dextran sulfate (DXS) and dextran were not effective. In combination with 200 nmol DDA, the optimal dose of antigen was 5 nmol A-PE, while at higher antigen doses DTH was diminished. Responses on combinations of 2 **adjuvants** and A-PE revealed that DXS counteracted the stimulatory effects of both DDA and CP-20,961. In vitro,

DDA formed insol. complexes with [14C]A-PE and at optimal antigen concn. >90% of the antigen was bound to the **adjuvant**. The percentage of [14C]A-PE bound to 200 nmol DDA decreased with increasing doses of [14C]A-PE. Addn. of DXS to the mixt. of [14C]A-PE and DDA reduced the percentage of [14C]A-PE bound to DDA. Dose-response curves demonstrated a close relationship between the inhibitory effects of DXS on the DTH and the A-PE/DDA complex formation. Nonsulfated dextran affected neither the DTH nor the formation of complexes in vitro. Thus, cellular adjuvanticity of DDA for the lipophilic antigen A-PE is probably the result of formation of insol. complexes with the antigen. Free A-PE suppresses the cellular response to A-PE/DDA complexes. The **adjuvant** DXS inhibits DTH by reducing the amt. of immunogenic A-PE/DDA complexes and thus increasing the amt. of free, immunosuppressive A-PE.

L7 ANSWER 57 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 20
1986:526981 Document No. 105:126981 Cyclophosphamide and dimethyldioctadecylammonium bromide immunopotentiate the delayed-type hypersensitivity response to inactivated enveloped viruses. Smith, R. H.; Ziola, B. (Dep. Microbiol., Univ. Saskatchewan, Saskatoon, SK, Can.). Immunology, 58(2), 245-50 (English) 1986. CODEN: IMMUAM. ISSN: 0019-2805.

AB Immunization of BALB/c mice with measles virus inactivated with .beta.-propiolactone and mixed with 100 .mu.g of the cationic surface-active lipid dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**] primes for a strong virus-specific delayed-type hypersensitivity (DTH) response that peaks 1 wk later. Optimal immunization and challenge doses were 8 and 4 .mu.g/mouse, resp., and pretreatment with 200 mg cyclophosphamide [50-18-0]/kg 2 days prior to immunization enhanced the DTH response. When compared to Freund's complete and incomplete **adjuvants**, DDA was superior for induction of DTH to inactivated purified measles virus. As DDA could be administered to animals at a site different from the measles virus antigens, or 1 day previously, and still enhance the DTH response, DDA probably acts more as an immune modulator than as a simple **adjuvant**. The conditions for an optimal DTH response to measles virus were also applicable to other enveloped viruses, for example, a strong DTH response was similarly generated to inactivated purified influenza PR8 virus and to herpes simplex virus type 1 antigens present in plasma membranes isolated from infected Vero cells.

L7 ANSWER 58 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 21
1986:440609 Document No. 105:40609 A new, sensitive assay to determine immunological **adjuvant** activity based on the immunogenicity of neuraminidase-treated sheep erythrocytes. Van Dijk, Hans; Rademaker, Pieternel M.; Klerx, Jac P. A. M.; Beukelman, Cees J.; Willers, Jan M. N. (Lab. Microbiol., State Univ. Utrecht, Neth.). Methods Find. Exp. Clin. Pharmacol., 8(3), 189-93 (English) 1986. CODEN: MFEPDX. ISSN: 0379-0355.

AB A novel, sensitive system to det. immunol. **adjuvant** activity is presented. It is based on the direct hemagglutinin response of mice to neuraminidase-treated sheep red blood cells (asialo-SRBC) 7 days after i.p. immunization. For 2 model **adjuvants**, the response was more sensitive to stimulation than that to normal SRBC. Optimal stimulatory activity was measured at an antigen dose of 3 .times. 106 asialo-SRBC. Using this dose, stimulation indexes up to 100 were obsd. The minimal ED

of dextran sulfate, the most potent **adjuvant** tested, was only 1 .mu.g. In addn. to substances with a rather general **immunostimulatory** activity, compds. with adjuvanticity that is commonly restricted to cellular responses were also effective in the system. The latter and reduced activity of the model **adjuvants** in nude mice strongly suggest that adjuvanticity in the asialo-SRBC model is T cell-dependent. Suppression of **adjuvant** activity in cobra venom factor-pretreated animals may indicate an involvement of complement in extrinsic **immunostimulatory** activity. Results show that the asialo-SRBC model is very suitable for evaluation and mechanistic study of immunol. **adjuvant** activity.

L7 ANSWER 59 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 22
1986:588946 Document No. 105:188946 Potentiation of the cellular immune response by **adjuvants**: a limited role for **adjuvant** induced interferon. Kraaijeveld, C. A.; Kamphuis, W.; Benaissa-Trouw, B. J.; Van Haarlem, H.; Harmsen, M.; Snippe, H. (Lab. Microbiol., State Univ. Utrecht, Utrecht, NL-3511 GG, Neth.). Int. Arch. Allergy Appl. Immunol., 81(2), 148-55 (English) 1986. CODEN: IAAAAM. ISSN: 0020-5915.

AB **Adjuvants** differ in their capacity to induce interferon (IFN). As a consequence, IFN induction by **adjuvants** may influence their effectiveness in enhancement of delayed-type hypersensitivity (DH) reactions. In this study, the lipophilic amine di-Me dioctadecyl ammonium bromide (DDA), the synthetic double-stranded polynucleotide polyinosinic polycytidylic acid (poly I:C), liposomes, and the polyols L 101 and L 121 were compared in BALB/c mice as inducers of IFN and also as **adjuvants** for DH to both lysozyme and inactivated Semliki Forest virus (SFV). The antigens were injected intracutaneously, alone or mixed with **adjuvant**. At day 6 after the immunization, DH was elicited and measured 24 h later as an increase in footpad thickness. Neg. charged liposomes and polyol L 121 were unable to enhance DH to SFV and also lack the capacity to induce IFN. Polyol L 101 induced low levels of IFN and showed only slight adjuvanticity for DH to SFV. In contrast, DDA, a moderate IFN inducer, was a very effective **adjuvant** for induction of DH against both lysozyme and SFV. The excellent IFN inducer, poly I:C, at the tested dose range (0.03-3.0 mg/kg), displayed only a relatively weak **adjuvant** activity. However, low doses of poly I:C (0.03 and 0.1 mg/kg) still showed adjuvanticity in contrast to the same doses of DDA. This might be related to sufficient induction of IFN by low doses of poly I:C but not by DDA. The discrepancy obsd. in the relation between IFN induction and a maximal DH induction suggests that IFN is not the only factor which enhances the effectiveness of **adjuvants** in induction of DH. Furthermore, various inbred mouse strains display considerable differences in DDA-induced enhancement of DH to both lysozyme and SFV, whereas no differences in DDA-induced IFN titers were detected. Thus, the capacity of an **adjuvant** to induce IFN is an important feature to achieve enhancement of DH reactions. The effectiveness of an **adjuvant**, however, is also detd. by its other intrinsic properties and by factors detd. by the host.

L7 ANSWER 60 OF 103 CAPLUS COPYRIGHT 2000 ACS
1985:594725 Document No. 103:194725 Modulation of **adjuvant**-enhanced delayed-type hypersensitivity by the interferon inducers poly I:C and Newcastle disease virus. Kraaijeveld, C.A.; Kamphuis, W.; Benaissa-Trouw, B. J.; Harmsen, M.; Snippe, H. (Lab. Microbiol., State

Univ. Utrecht, Utrecht, NL-3511, Neth.). Int. Arch. Allergy Appl. Immunol., 79(1), 86-9 (English) 1986. CODEN: IAAAAM. ISSN: 0020-5915.

AB The modulation by the interferon (IFN) inducers poly I:C and Newcastle disease virus (NDV) of the effector phase of **adjuvant**-enhanced delayed-type hypersensitivity (DH) was studied in mice. A strongly enhanced DH was induced in mice to UV light inactivated Semliki forest virus (SFV) by the use of the **adjuvant** dimethyldioctadecylammonium bromide. At day 6 after intracutaneous immunization, DH was elicited with SFV and measured 24 and 48 h later as increase in footpad thickness (footpad swelling test). Systemic, i.v. administration of either poly I:C, UV-inactivated NDV, or NDV-induced IFN prior to elicitation of DH with antigen resulted in a temporarily suppressed DH reaction. Both the poor swelling at 3 h and strong swelling at 24 h were suppressed, while the swelling at 48 h was enhanced. The model described provides a sensitive in vivo method to study modulating effects of drug and microbial agents on the effector phase of DH.

L7 ANSWER 61 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 23

1987:117931 Document No. 106:117931 Dissociation between enhanced resistance and delayed hypersensitivity induced with subcellular preparations from Listeria monocytogenes and the **adjuvant** dimethyldioctadecyl-ammonium bromide. Antonissen, A. C. J. M.; Lemmens, P. J. M.; Van den Bosch, J. F.; Van Boven, C. P. A. (Dep. Med. Microbiol., Univ. Limburg, Maastricht, 6200 MD, Neth.). Antonie van Leeuwenhoek, 52(1), 75-84 (English) 1986. CODEN: ALJMAO. ISSN: 0003-6072.

AB The relation between enhanced resistance and delayed hypersensitivity (DH) induced with subcellular prepns. from L. monocytogenes and the **adjuvant** dimethyldioctadecylammonium bromide (DDA) was investigated. RRNA as well as cell envelope fragments (fraction I) protected mice against lethal Listeria infection. However, only fraction I induced DH against killed Listeria. For the induction of protection with fraction I or RNA as well as for the induction of DH with fraction I, prepns. had to be administered in combination with DDA. Fraction I elicited a DH response in mice immunized with viable Listeria, but RNA did not. These observations pointed to a dissocn. between DH and enhanced resistance induced with RNA, and to a dissocn. between fraction I and RNA with respect to their ability to induce or elicit DH. Also DH and enhanced resistance induced with fraction I could be dissocd. Intracutaneous administration of fraction I induced high levels of DH without concomitant induction of protection against lethal challenge with Listeria. On the other hand, i.p. administration of fraction I fully protected mice against lethal infection, but only induced a moderate DH response. DH induced with fraction I was largely specific, whereas enhanced resistance induced with this prepn. was nonspecific. Finally, proteinase K-sensitive proteins were essential for the induction of DH but not for the induction of protection with fraction I.

L7 ANSWER 62 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 24

1986:146832 Document No. 104:146832 Effects of immunological **adjuvants** on the mouse complement system. II. Anti-complementary effects of surface-active compounds. Klerx, Jac P. A. M.; Van Dijk, Hans; Kouwenberg, Erik A.; Van der Maaden, Walter J.; Willers, Jan M. N. (Med. Fac., State Univ. Utrecht, Utrecht, Neth.). Int. J. Immunopharmacol., 8(1), 47-52 (English) 1986. CODEN: IJIMDS. ISSN: 0192-0561.

AB The anti-complementary effects of the surface-active immunol. **adjuvants** dimethyldioctadecylammonium bromide (DDA) and pluronic polyols L101 and L121 were investigated in a mouse system. All 3 **adjuvants** showed complement (C)-inactivating effects. DDA caused a time-dose-dependent redn. of alternative pathway (AP) and overall C activity, which varied with the serum concn. Polyols induced a preferential inactivation of the AP by a more direct mechanism. A rather general, causative relationship between anti-complementary and immunol. **adjuvant** activities is suggested. This might involve interference with nonspecific elimination of antigen, counteraction of immunosuppression by terminal C components, and/or moderation of C3b-mediated redn. of Ia-expression, leading to a better antigen presentation.

L7 ANSWER 63 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 25
1987:31274 Document No. 106:31274 Transfer of enhanced resistance against Listeria monocytogenes induced with ribosomal RNA and the **adjuvant** dimethyldioctadecylammonium bromide. Antonissen, A. C. J. M.; Lemmens, P.
J. M. R.; Van den Bosch, J. F.; Van Boven, C. P. A. (Dep. Med. Microbiol., Univ. Limburg, Maastricht, 6200 MD, Neth.). Immunol. Lett., 14(1), 21-8 (English) 1986. CODEN: IMLED6. ISSN: 0165-2478.
AB The mechanism of enhanced resistance against Listeria monocytogenes induced with Listeria rRNA and the **adjuvant** dimethyldioctadecylammonium bromide (DDA) was investigated. Mice immunized with DDA alone (which were not protected against Listeria-infection) were used as neg. controls. Mice immunized with RNA plus DDA had an increased capacity to mobilize polymorphonuclear leukocytes (PMNs) and macrophages to the inflamed peritoneal cavity compared to mice immunized with **adjuvant** alone. I.p. inflammation was induced by injection of sterile irritant proteose peptone. The protective capacity of various cell-populations was investigated by i.p. transfer of cells to normal recipient mice and concomitant challenge of recipient animals with a LD of viable Listeria. Inflammatory PMNs as well as inflammatory macrophages from mice immunized with RNA plus DDA protected recipient animals against listeriosis whereas cells from mice immunized with DDA alone failed to do so.

L7 ANSWER 64 OF 103 CAPLUS COPYRIGHT 2000 ACS
1985:571549 Document No. 103:171549 The serologic response to Meth A sarcoma vaccines after cyclophosphamide treatment is additionally increased by various **adjuvants**. Livingston, Philip O.; Jones, Michele; Deleo, Albert B.; Oettgen, Herbert F.; Old, Lloyd J. (Mem. Sloan-Kettering Cancer Cent., New York, NY, 10021, USA). J. Immunol., 135(2), 1505-9 (English) 1985. CODEN: JOIMA3. ISSN: 0022-1767.
AB The serol. response of BALB/c mice to immunization with BALB/c sarcoma Meth A cells was more effectively augmented by pretreatment with cyclophosphamide (Cy) [50-18-0] than by the use of **adjuvants**. The serol. response was directed against a highly restricted cell surface antigen, closely related to or identical with the unique transplantation antigen characteristic for this tumor. Attempts to obtain addnl. augmentation by using Cy and **adjuvants** together were made. For these studies, the optimal Cy dose, interval between Cy and vaccine administration, and vaccine cell no. were detd. Mice were injected with Cy (25 mg/kg, i.p.) and 3 days later, with viable irradiated (10,000 rad) Meth A cells s.c., under conditions in which only few mice produced antibody. Sera were tested for antibody with reactivity against Meth A by

complement dependent cytotoxicity (CDCX), which predominantly detects IgM,
and by the protein A (PA) and anti-IgG assays, which detect IgG. Of the various **adjuvants** tested, only monophosphoryl lipid A(MPLA)and CP 20961 [35607-20-6] resulted in significantly increased titers of reactivity in both the CDCX and PA assays over that obtained when using Cy
alone. Although the mean titers obsd. CDCX ranged between 1/160 and 1/320, no titer above 1/40 was obsd. with the PA assay. The specificity of the CDCX reactivity detected by the assay for the Meth A antigen was ascertained by absorption anal. of selected sera by using a panel of BALB/c spleen and tumor cell lines grown in vitro or in vivo. PA titers were too low to permit absorption anal., and the titers obtained in the anti-IgG assay were lower still. Attempts to augment the anti-Meth A IgG response or to convert the IgM response to IgG were unsuccessful. The combined approach described here (i.e., vaccination with irradiated syngenetic tumor cells plus MPLA in cy-pretreated mice) was also shown to be effective in agumenting the serol. response against 2 addnl. murine leukemia virus-neg. sarcomas that are known to be less immunogenic, CMS4 and CMS5. This combined approach may be applicable to stimulating serol. responses against a variety of tumor cell surface antigens.

L7 ANSWER 65 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1986:142661 Document No.: BA81:53077. ANTIBACTERIAL RESISTANCE MACROPHAGE INFLUX AND ACTIVATION INDUCED BY BACTERIAL RIBOSOMAL RNA WITH DIMETHYLDIOCTADECYLAMMONIUM BROMIDE. GONGGRIJP R; MULLERS W J H A; DULLENS
H F J; VAN BOVEN C P A. DEP. MED. MICROBIOL., UNIV. LIMBURG, MAASTRICHT, NETH.. INFECT IMMUN, (1985) 50 (3), 728-733. CODEN: INFIBR. ISSN: 0019-9567. Language: English.
AB Intraperitoneally injected rRNA from Pseudomonas aeruginosa combined with dimethyldioctadecylammonium bromide (DDA) increased nonspecifically the resistance of mice against an intraperitoneal challenge with extracellular
(P aeruginosa, Escherichia coli) and intracellular (Listeria monocytogenes) bacteria. This study concerns the mechanism underlying the nonspecific resistance. RNA with DDA (RNA-DDA) induced a study concerning the mechanism underlying the nonspecific resistance. RNA with DDA (RNA-DDA) induced a cell influx and activated peritoneal macrophages (M.PHI.) as judged by the decreased 5'-nucleotidase and alkaline phosphodiesterase activities in M.PHI. lysates, the enhanced O2- release, and the increased antitumor activity in comparison with unstimulated M.PHI.. RNA without DDA did not enhance the resistance and did not influence the peritoneal cell numbers or M.PHI. properties. DDA without RNA enhanced the resistance of mice only slightly; it induced a cell influx, yielding elicited M.PHI. as judged by the decreased 5'-nucleotidase activity and increased alkaline phosphodiesterase activity, the slightly enhanced O2- release, and the absence of increased antitumor activity. Both RNA-DDA and DDA M.PHI. showed an enhanced capacity to ingest and kill L. monocytogenes in vitro, DDA M.PHI. being slightly less effective than RNA-DDA M.PHI. with respect to killing. We conclude that the enhanced killing capacity of M.PHI. for L. monocytogenes
is characteristic of both elicited DDA M.PHI. and activated RNA-DDA M.PHI.. The relationship between nonspecific resistance, peritoneal cell numbers, and antibacterial M.PHI. activity is discussed. In addition, it is shown that RNA and DDA retain their activity when they are injected apart, suggesting that they activate M.PHI. by sequential action.

L7 ANSWER 66 OF 103 CAPLUS COPYRIGHT 2000 ACS
1985:612920 Document No. 103:212920 RNase-sensitive and RNase-insensitive

protective components isolated from Listeria monocytogenes. Antonissen, A. C. J. M.; Lemmens, P. J. M. R.; Gonggrijp, R.; Van den Bosch, J. F.; Van Boven, C. P. A. (Dep. Med. Microbiol., Univ. Limburg, Maastricht, 6200
MD, Neth.). Antonie van Leeuwenhoek, 51(2), 227-40 (English) 1985. CODEN: ALJMAO. ISSN: 0003-6072.
AB Crude ribosomes were isolated from L. monocytogenes serotype 4b and sepd. into 2 fractions by mol. sieve chromatog. Chem. anal. indicated that fraction I contained cell envelope components while fraction II contained the ribosomes. Both fractions protected mice against Listeria, but only in combination with the **adjuvant** dimethyldioctadecylammonium bromide (DDA). RNase-treatment, but not proteinase K-treatment, destroyed
the protective properties of fraction II, and RNA purified from fraction II also induced protection. Protection induced by fraction I was not affected by either RNase- or proteinase K-treatment. Both s.c. and i.p., but not i.v., administration of fraction I, fraction II, or purified RNA induced significant protection against i.p. infection, the i.p. route of administration being the most effective. All prepns. induced high levels of protection 3 to 7 days after administration, but protection was already
decreased after 14 days. Protection induced with RNA appeared to be biphasic, because it also protected mice 1 day, but not 2 days after administration. Protection induced with both fraction I and RNA was at least in part nonspecific, because both prepns. also protected mice against L. monocytogenes serotype 3, Streptococcus pneumoniae, and Pseudomonas aeruginosa. Results are discussed in relation to previous work with analogous prepns. from P. aeruginosa.

L7 ANSWER 67 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 26
1985:498416 Document No. 103:98416 Effect of dimethyldioctadecylammonium bromide induced macrophages on malignant cell proliferation. Prager, Morton D.; Kanar, Melissa C.; Farmer, Jeffrey L.; Vanderzee, John (Health Sci. Cent., Univ. Texas, Dallas, TX, 75235, USA). Cancer Lett. (Shannon, Irel.), 27(2), 225-32 (English) 1985. CODEN: CALEDQ. ISSN: 0304-3835.
AB Murine peritoneal macrophages elicited by dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**] which is a potent immune **adjuvant**, were examd. for cytotoxic and growth inhibiting activity for malignant cells. DDA macrophages had no cytolytic activity for murine
B16BL-6 melanoma or human SMS-SB pre-B leukemia cells even in the presence
of up to 1 .mu.g bacterial endotoxin (lipopolysaccharide, LPS)/mL. However, they exhibited a variable inhibitory effect on the growth of several lines of leukemia cells. The no. of SMS-SB and human NALL remained essentially static in the presence of DDA macrophages while they increased significantly when cultured with resident macrophages. In contrast, L1210 cells increased 5-8-fold in the presence of macrophages elicited either by DDA or the inflammatory agent proteose peptone (PP). Although DDA macrophages retarded L1210 growth relative to PP macrophages,
both populations responded to LPS in a comparable dose-dependent manner to
become essentially cytostatic at 1 .mu.g LPS/mL.

L7 ANSWER 68 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1985:388496 Document No.: BA80:58488. POTENTIATING EFFECT OF **ADJUVANTS** ON HUMORAL IMMUNITY TO PORCINE PARVOVIRUS VACCINES IN GUINEA-PIGS. MOLITOR
T W; JOO H S; THACKER B J. DEP. LARGE ANIMAL CLINICAL SCI., COLLEGE VET. MED., UNIV. MINN., ST. PAUL, MN 55108, USA.. VET MICROBIOL, (1985) 10 (3),

209-218. CODEN: VMICDQ. ISSN: 0378-1135. Language: English.
AB Fourteen different **adjuvants**, given either in single or combined form with another compound, were compared in guinea pigs for their ability to potentiate humoral immunity to porcine parvovirus (PPV) antigen after 2 vaccinations. Two injections were given, the second 3 wk following the initial vaccination. Antibody concentrations to PPV in sera from injected animals were measured over a 5-wk period by the hemagglutination inhibition (HI) test. At the conclusion of the experiment, guinea pigs injected with the following **adjuvants** and PPV antigen: CP-20 961 (Avridin), 50% aluminum hydroxide gel, ethylene maleic anhydride (EMA), oil and water emulsion (O/W) and dimethyldioctadecylammonium bromide (DDA) immunologically responded with high geometric mean HI titers (380, 224 and 427, 602, 512, 1202, respectively), whereas guinea pigs receiving Emulsan, sodium dodecyl sulfate (SDS), L-121, combinations of Emulsan/aluminum hydroxide, SDS/aluminum hydroxide and Bordetella pertussis/aluminum hydroxide responded with low mean titers (54, 64, 18, 27, 11, 64, 14, 20, respectively). Guinea pigs injected with antigen without **adjuvant** responded weakly with geometric mean titers of 3.3 and 16 for the 2 groups tested. Prior to booster injection, guinea pigs immunized with 13 of the preparations had low (< 4) or undetectable antibody titers. Antibody titers from guinea pigs receiving DDA **adjuvant** continued to rise throughout the duration of the experiment and at the conclusion had the highest mean titers of the groups tested (1202). The 2 groups immunized with 50% aluminum hydroxide gel had high mean titers (224, 427), but in both instances there was a wide range of titers within a group evidenced by high standard antibody titers within a group evidenced by high standard deviations. In contrast, guinea pigs receiving either DDA, CP-20 961, O/W or EMA had antibody titers within a narrow range and small SD. The significance of aluminum hydroxide gel concentration on immunogenicity is discussed.

L7 ANSWER 69 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 27
1985:571556 Document No. 103:171556 Muramyl dipeptide analogs as potentiators of the antitumor action of endotoxin. Bloksma, Nanne; Hofhuis, Frans M. A.; Willers, Jan M. N. (Dep. Immunol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Cancer Immunol. Immunother., 19(3), 205-10 (English) 1985. CODEN: CIIMDN. ISSN: 0340-7004.
AB The potentiation of endotoxin-induced necrosis and regression of solid syngeneic Meth A tumors in mice previously obsd. following administration of muramyl dipeptide (MDP) [53678-77-6] was investigated further by use of various muramyl peptide analogs and 2 unrelated synthetic **adjuvants**, the pluronic polyol L121 [9003-11-6] and dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**]. All agents were administered in aq. soln. by the i.v. route. None of the muramyl peptide analogs nor L121 or DDA had any strong antitumor action of their own. Two 6-O-acylated muramyl peptides (L2-MDP [66996-40-5] and B30-MDP [66880-80-6]) and muramyl dipeptide stearoylsine [MDP-Lys (L18)] [78113-36-7] clearly potentiated endotoxin-induced necrosis and regression. In contrast, MDP with L- instead of D-isoglutamine was completely inactive. Optimal activity of B30-MDP and MDP-Lys (L18) was only achieved by adding of suitable amts. of a nonionic surfactant. L121 and DDA could not replace muramyl peptides as potentiating agent. The combination of endotoxin, MDP, and L121 caused complete tumor regression

in all mice, but ws highly toxic. On the basis of the data in the literature on the biol. response-modifying activities of the agents used, it is concluded that the potentiating activity of muramyl peptides cannot yet be related to their immunoadjuvant action or their capacity to activate macrophages or to enhance nonspecific bacterial resistance.

L7 ANSWER 70 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 28
1985:219338 Document No. 102:219338 Combinations of two synthetic **adjuvants**: synergistic effects of a surfactant and a polyanion on the humoral immune response. Hilgers, Luuk A. T.; Snippe, Harm; Jansze, Margriet; Willers, Jan M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Cell. Immunol., 92(2), 203-9 (English) 1985. CODEN: CLIMB8. ISSN: 0008-8749.
AB Synergistic effects of 2 synthetic **adjuvants**, dimethyldioctadecylammonium bromide (DDA) and dextran sulfate (DXS) on the humoral response to sheep red blood cells (SRBC) were investigated. Mice received i.p. injections of **adjuvant** and antigen simultaneously. The no. of plaque-forming cells (PFC) in the spleen were detd. 5 days later and circulating anti-SRBC antibodies were measured till 16 wk after immunization. Although combinations of DDA and DXS were very effective in enhancing the PFC response to both moderate (2 .times. 107) and low (2 .times. 106) doses of SRBC, synergy between the **adjuvants** was only obsd. at the low dose of SRBC. Optimal augmentation of the primary response to the low antigen dose was evoked by the combination of the highest dose tested to either **adjuvant** (1 .mu.mol DDA and 1 nmol DXS) resulting in a 560-fold increase of the no. of PFC in the spleen as compared to controls. Even combinations of relatively small amts. of both **adjuvants** were very effective in augmenting the response to SRBC. Mice receiving half the amts. of both **adjuvants** with 2 .times. 106 SRBC displayed increased nos. of PFC in the spleen at day 5 as well as increased titers of total anti-SRBC antibodies at week 1 and week 2 and 2-mercaptoethanol-resistant antibodies from week 4 till week 16 as compared to the calcd. sum of responses in mice which received either DDA (0.05 .mu.mol per mouse) or DXS (0.05 nmol per mouse). The mechanism behind the synergy between these **adjuvants** is discussed and the possibility of discerning **adjuvants** on their modes of action is suggested.

L7 ANSWER 71 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 29
1985:420864 Document No. 103:20864 Effect of in vivo administration of different **adjuvants** on the in vitro candidacidal activity of mouse peritoneal cells. Hilgers, Luuk A. T.; Snippe, Harm; Jansze, Margriet; Willers, Jan M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, Neth.). Cell. Immunol., 90(1), 14-23 (English) 1985. CODEN: CLIMB8. ISSN: 0008-8749.
AB The candidacidal activity (CA) of peritoneal cells (PC) in vitro was used as a measure of nonspecific microbial activity of phagocytes after i.p. injection of mice with different **adjuvants**. Dilns. of PC were incubated with const. nos. of Candida parapsilosis in a 96-well culture plate. The PC no. causing 50% redn. of yeast colonies formed after 48 h at 37.degree. was called 1 CA50 unit. CA was expressed in CA50 units per 106 PC. Optimal redn. of the no. of viable candida cells in vitro was established within 1.5 h while 50% redn. was reached after 0.5 h. In this test, CA was, within limits, independent of the no. of viable candida cells added per well (22-152 yeast cells), of the concn. of fetal calf serum (1-20%), and of the presence of heat-labile serum components. The

CA of PC of individual mice was measured 6, 24, and 96 h after injection of an **adjuvant**. In most instances optimal CA was obsd. 6 h after administration of **adjuvant** and varied from 3.7 (methylamine) to 50 (Corynebacterium parvum strain 4982) units. With respect to the titer and duration of CA, the **adjuvants** were arranged in the following order of increasing efficacy: methylamine, heparin, polyol L 121, suramin, dextran sulfate, polyol L 101, dimethyldioctadecylammonium bromide, Liquoid, heat-killed Listeria monocytogenes, formalin-killed C. parvum strain 10387, and strain 4982. The CA induced by the latter strain persisted at least until 96 h after injection. The induction of CA was accompanied by recruitment of polymorphonuclear cells. The contribution of distinct phagocytic effector cells to CA and the correlation between modulation of the specific and nonspecific immunity are discussed.

L7 ANSWER 72 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1985:324857 Document No.: BA79:104853. RNASE-SENSITIVE RIBOSOMAL VACCINES. GONGGRIJP R; ANTONISSEN A C J M; VAN DEN BOSCH J F; VAN BOVEN C P A. DEP. MED. MICROBIOL., UNIV. LIMBURG, P.O. BOX 616, 6200 MD MAASTRICHT, THE NETH.. ANTONIE LEEUWENHOEK J MICROBIOL, (1984 (RECD 1985)) 50 (5-6), 763-774. CODEN: ANLEDR. Language: English.

AB This analysis of the protective properties of the components in RNase sensitive ribosomal vaccines, in particular the RNA. The protective activities in mice of purified ribosomes derived from Pseudomonas aeruginosa and from Listeria monocytogenes were compared. Both ribosomal vaccines had to be combined with the **adjuvant** dimethyldioctadecylammonium bromide (DDA) in order to be protective, and both lost their activity after RNase treatment. The ribosomal vaccines as well as RNA purified from the ribosomes induced non-specific protection. Injection i.p. of RNA with DDA induced an influx of peritoneal cells. RNA with DDA activated macrophages enhanced phagocytic activity and killing capacity for L. monocytogenes. The results suggest that the observed macrophage activation is probably T-cell-independent. With regard to the ribosomal vaccine of P. aeruginosa it is concluded that RNA also contributed to the protective activity by increasing the humoral response against suboptimal concentrations of contaminating cell surface antigens. Evidently, ribosomal vaccines may be considered as a combination of a non-specific immunomodulator (RNA) with pathogen-specific cell surface antigens. This concept of ribosomal vaccines is discussed in relation to the literature concerning RNase-sensitive ribosomal vaccines.

L7 ANSWER 73 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 30
1984:452963 Document No. 101:52963 Immunomodulating properties of two synthetic **adjuvants**: dependence upon type of antigen, dose, and time of administration. Hilgers, Luuk A. T.; Snippe, Harm; Jansze, Margriet; Willers, Jan M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Cell. Immunol., 86(2), 393-401 (English) 1984. CODEN: CLIMB8. ISSN: 0008-8749.

AB The effects of 2 synthetic **adjuvants** on the antibody response to sheep red blood cells (SRBC) as a thymus dependent (TD) antigen and to dinitrophenyl59-Ficoll as a thymus-independent antigen were investigated in mice. Both dimethyldioctadecylammonium bromide (DDA) and dextran sulfate (DXS) augmented the humoral response to SRBC but not to dinitrophenyl59-Ficoll if injected simultaneously with antigen. Dose-response curves of both antigen and **adjuvant** revealed that DXS compared to DDA is a more effective **adjuvant** for the induction of a humoral response to SRBC. I.p. injection of DDA or DXS evoked a sequence of distinct immune responsive states in mice, measured by the capacity to develop an anti-SRBC response. A short immune-potentiating period (<6 h) is followed by a suppressive, second

immune-potentiating state. The immune suppressive state lasted for a period of about 8 days and was restricted to TD-antigens. Suppression could be totally overridden by injection of DDA or DXS simultaneously with antigen, suggesting that the suppressive state was reversible. The kinetics of the obsd. alteration of the immune response by DDA and DXS were very similar. It is concluded that differences in the modulation of the immune response by DDA and DXS are limited to the initial state. Long-term effects like the induction of a succession of distinct immune responsive states, are more or less similar for both **adjuvants**. Possible mechanisms by which these immunomodulators interfere with the immune system are discussed.

L7 ANSWER 74 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1984:339528 Document No.: BA78:76008. **ADJUVANT** REQUIREMENTS FOR PROTECTIVE IMMUNIZATION OF MICE USING A TRYPANOSOMA-CRUZI 90 KILODALTON CELL SURFACE GLYCO PROTEIN. SCOTT M T; BAHR G; MODDABER F; AFCHAIN D; CHEDID L. DEP. OF EXPERIMENTAL IMMUNOBIOL., WELLCOME RES. LAB., LANGLEY COURT, BECKENHAM, KENT, BR3 3BS U.K.. INT ARCH ALLERGY APPL IMMUNOL, (1984) 74 (4), 373-377. CODEN: IAAAAM. ISSN: 0020-5915. Language: English.
AB A wide range of **adjuvants** including alhydrogel, saponin, Corynebacterium parvum [Propionibacterium acnes] DDAB [dimethyldioctadecyl-ammonium bromide] Pfizer CP-20,961 [N,N-dioctadecyl-N',N'-bis(2-hydroxyethyl)propanediamine], oil **adjuvants** [squalane] and several MDP [muramyl dipeptide] analogs [327, 337, 341, 342] were compared for their **adjuvant** activity in protecting mice against lethal T. cruzi infection following immunization with a T. cruzi 90K [Kilodalton] cell surface glycoprotein. Only saponin was effective. Promotion did not correlate with the ability to promote a particular Ig isotype; however, saponin was unique in its ability to promote cell-mediated immunity against the 90K glycoprotein.

L7 ANSWER 75 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1984:291224 Document No.: BA78:27704. DELAYED TYPE HYPER SENSITIVITY AGAINST SEMLIKI-FOREST VIRUS IN MICE LOCAL TRANSFER OF DELAYED TYPE HYPER SENSITIVITY WITH THIO GLYCOLATE INDUCED PERITONEAL EXUDATE CELLS. KRAAIJEVELD C A; BENAISSA-TROUW B; HARMSEN M; SNIPPE H. LAB. MICROBIOL., STATE UNIV. UTRECHT, CATHARIJNESINGEL 59, NL-3511 GG UTRECHT.. INT ARCH ALLERGY APPL IMMUNOL, (1984) 73 (4), 342-346. CODEN: IAAAAM. ISSN: 0020-5915. Language: English.
AB In mice, a strong delayed type hypersensitivity (DH) without detectable neutralizing antibodies in serum could be obtained after intracutaneous injection of inactivated Semliki Forest virus (SFV) mixed with the **adjuvant** dimethyl dioctadecyl ammonium bromide (DDA). Thioglycollate-induced peritoneal exudate cells (PEC) from these mice were highly effective in passive transfer of DH against SFV locally in footpads of naive recipient mice. DH reactions were measured with a footpad swelling test. Neither immune PEC from nonstimulated peritoneal cavities nor thioglycollate-induced PEC from mice which developed neutralizing antibodies were able to transfer DH passively.

L7 ANSWER 76 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 31
1983:610893 Document No. 99:210893 Effect of the **adjuvant** dimethyl dioctadecyl ammonium bromide on the humoral and cellular immune responses to encephalomyocarditis virus. Kraaijeveld, Cornelis A.; La Riviere, Geertje; Benaissa-Trouw, Barry J.; Jansen, Jaap; Harmsen, Theo; Snippe,

Harm (Lab. Microbiol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Antiviral Res., 3(3), 137-49 (English) 1983. CODEN: ARSRDR. ISSN: 0166-3542.

AB The effects of the **adjuvant** di-Me dioctadecyl ammonium bromide (DDA) on the immune responses to encephalomyocarditis (EMC) virus were studied in mice. The humoral response, as measured by appearance of neutralizing antibodies, was slightly enhanced in mice immunized by the i.p. route. Intracutaneously, DDA almost did not affect the humoral response but resulted in distinct enhancement of delayed type hypersensitivity (DH), as measured by the footpad swelling test. DH to EMC virus was antigen-specific and could be passively transferred to normal mice with peritoneal exudate cells from immunized mice. Dose-response curves for DH and humoral antibody responses to EMC virus were not concordant. Low doses induced DH on day 6 without measurable circulating antibodies; high doses gave good antibody responses but suboptimal DH reactions. Immunization conferred a state of resistance to infection with virulent EMC virus. Protection seemed more related to DH than to the prevalence of specific antibodies at the time of infection.

L7 ANSWER 77 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 32

1983:515724 Document No. 99:115724 Impaired macrophage functions as a possible basis of immunomodification by microbial agents, tilorone and dimethyldioctadecylammonium bromide. Bloksma, Nanne; De Reuver, Marinus J.; Willers, Jan M. N. (Lab. Microbiol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Antonie van Leeuwenhoek, 49(1), 13-22 (English) 1983. CODEN: ALJMAO. ISSN: 0003-6072.

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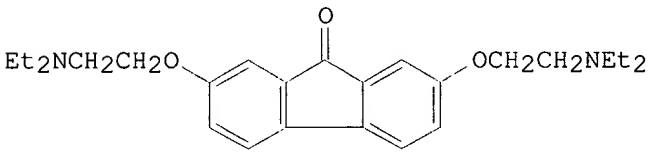

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AB Four microbial and two chem. defined immunomodulating agents namely viable BCG, killed Mycobacterium butyricum, killed Lactobacillus plantarum, zymosan tilorone (I) [27591-97-5] and dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**] were studied for their effects on macrophage functions in vitro and in vivo. All agents induced a dose-dependent mortality of macrophages as detd. by trypan blue exclusion. DDA and esp. tilorone were rather toxic for macrophages in vitro. All agents except tilorone and DDA inhibited phagocytosis of yeast cells and uptake of acridine orange in vitro at doses which killed up to .apprx.30% of the macrophages. DDA and tilorone had no effect at similar doses. All agents but zymosan inhibited the spreading of macrophages. No interference with the fusion of lysosomes and yeast cell-contg. phagosomes could be obsd. The activity of the mononuclear phagocytic system in vivo was stimulated by all substances within 24 h. All agents but DDA and tilorone enhanced non-specific bacterial resistance. As demonstrated previously for DDA, tilorone could serve as **adjuvant** for induction of specific resistance to Listeria monocytogenes. The results are discussed in relation to other data on influencing of macrophage functions and on immunomodification. Thus, hampered antigen destruction by local macrophage suppression attended with MPS stimulation might be a basic

mechanism for adjuvanticity exerted by these agents.

L7 ANSWER 78 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 33
1983:32686 Document No. 98:32686 Interaction of antigens with dimethyldioctadecylammonium bromide, a chemically defined biological response modifier. Baechtel, F. Samuel; Prager, Morton D. (Health Sci. Cent., Univ. Texas, Dallas, TX, 75235, USA). Cancer Res., 42(12, Pt. 1), 4959-63 (English) 1982. CODEN: CNREA8. ISSN: 0008-5472.
AB Dimethyldioctadecylammonium bromide (DDA) stimulates immune responses, primes (or activates) macrophages, and binds to antigens. Because relatively little is known about the binding of **adjuvants** to antigens, the nature of the interaction of DDA with sol. protein and cellular antigens was investigated. Dose-dependent, stable complexes are formed between cells and the lipoidal cation of DDA. Since the interaction is independent of neg. charged sialic acid residues of the cell membrane and little DDA binds to intracellular structures, it is suggested that binding occurs primarily at the cell membrane, probably through hydrophobic interaction with lipids. The idea of membrane perturbation is supported by the leak of macromols. (lactate dehydrogenase) from treated cells. Reaction of varying amts. of DDA with a const. amt. of ovalbumin was also dose dependent. Because of a minimal effect of ionic strength on the reaction, it is concluded that ionic interaction may make a minor contribution to product formation. Complexes of DDA and antigen are particularly effective in eliciting a delayed hypersensitivity reaction, which has been postulated to be desirable for an antitumor effect.

L7 ANSWER 79 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1983:253192 Document No.: BA76:10684. PROLONGATION OF ACQUIRED CELLULAR RESISTANCE TO LISTERIA-MONOCYTOGENES. WILLERS J M N; HOFHUIS F M A; VAN DER MEER C. DEP. IMMUNOLOGY, LAB. MICROBIOL., CATHARIJNESINGEL 59, 3511 GG UTRECHT, NETHERLANDS.. IMMUNOLOGY, (1982) 46 (4), 787-792. CODEN: IMMUAM. ISSN: 0019-2805. Language: English.
AB Intracutaneous immunization of mice with 105 or 106 viable listeria resulted in acquired cellular resistance (ACR) of short duration (7 days) and in delayed-type hypersensitivity (DH) lasting at least 27 days. The ACR was partially non-specific; 50% of the mice were also protected against a lethal challenge with Salmonella enteritidis. The specific element of the ACR could be transferred by non-adherent spleen cells from immune mice to normal recipient mice. Such transfer was not possible with adherent spleen cells from immune mice or with spleen cells from normal mice. Two systems of multiple immunizations to extend the period during which mice were protected against a challenge with 50 LD50 of listeria were used. In the 1st system, mice were immunized with 106 viable listeria and subsequently challenged with 50 LD50 (107) of viable listeria. Mice surviving the challenge were actually boosted at the challenge injection for ACR. In the 2nd system, mice were immunized and boosted with 108 killed listeria mixed with the **adjuvant** dimethyl dioctadecyl ammonium bromide (DDA). In the former system, after each booster injection with viable listeria, the interval during which the mice were protected doubled and reached a maximum of 31 days. In the latter system, all intervals between 2 booster injections were equally long and never exceeded 28 days. In both systems, the existence of immunological memory was suggested. The difference in results obtained after immunization with viable listeria and killed listeria mixed with DDA are discussed.

L7 ANSWER 80 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 34

1983:214980 Document No.: BA75:64980. THE INDUCTION OF LYMPHOCYTES WITH THE CAPACITY TO RENDER MACROPHAGES CYTO TOXIC IN AN ALLOGENEIC MURINE SYSTEM. DE WEGER R A; PELS E; DEN OTTER W. DEP. PATHOL., PASTEURSTRAAT 2, 3511 HX UTRECHT, NETHERLANDS.. IMMUNOLOGY, (1982) 47 (3), 541-550. CODEN: IMMUAM. ISSN: 0019-2805. Language: English.

AB Sensitized [mouse] spleen and peripheral lymph node lymphocytes were tested, after different types of immunization with allogeneic tumor cells, for their capacity to induce macrophage cytotoxicity in vitro. The macrophages were rendered cytotoxic either by direct contact with lymphocytes and [mouse lymphoma SL2] tumor cells (activation of macrophages) or by a factor (macrophage arming factor, MAF), released by the sensitized lymphocytes incubated with tumor cells (arming of macrophages). Both types of reactions are T-cell dependent. Macrophage activation is a more sensitive way to detect lymphocytes with the capacity to render macrophages cytotoxic than arming of macrophages. The route of immunization s.c. or i.p. with allogeneic cells did not influence the induction of lymphocytes with the capacity to render macrophages cytotoxic. The tumour cells had to be intact as disrupted cells (suspended in Freunds complete **adjuvant**, FCA) did not induce macrophages activating lymphocytes. The **adjuvant** dimethyl dioctadecyl ammonium bromide (DDA) did not increase the lymphocyte response. Intact allogeneic tumor cells were needed in vitro when used for secondary antigenic stimulation. This secondary stimulation was independent of antigen presentation by macrophages. This suggests that in vivo the primary response is independent of macrophage antigen presentation. Delayed-type hypersensitivity and antibody responses against the allogeneic tumor cells were comparable after s.c. and i.p. immunization, and after immunization with FCA and DDA.

L7 ANSWER 81 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 35

1983:222763 Document No.: BA75:72763. A COMPARISON OF SAPONIN WITH OTHER **ADJUVANTS** FOR THE POTENTIATION OF PROTECTIVE IMMUNITY BY A KILLED PLASMODIUM-YOELII VACCINE IN THE MOUSE. MCCOLM A A; BOMFORD R; DALTON L. GLAXO GROUP RES. LIMITED, GREENFORD ROAD, GREENFORD, MIDDLESEX UB6 0HE, U.K.. PARASITE IMMUNOL (OXF), (1982) 4 (5), 337-348. CODEN: PAIMD8. ISSN: 0141-9838. Language: English.

AB The protective immunity conferred by s.c. injection of outbred CD-1 mice with a killed P. yoelii (YM strain) vaccine was strongly potentiated by saponin. By adjusting the dose of antigen, the number of immunizations and the number of living parasites in the challenge infection, conditions were defied where antigen alone was non-protective but 100% protection was obtained by the addition of saponin. Inbred BALB/c, CBA/CA and C57 Bl mice were much less responsive than the CD-1 mice. The following **adjuvants** were compared with saponin: mineral oil emulsions (Freund's incomplete and complete **adjuvants** [FCA]); Al(OH)3(Alhydrogel); bacteria and synthetic bacterial derivatives (Bordetella pertussis, Corynebacterium parvum and muramyl dipeptide); surface active materials (digitonin, vitamin A, Arquad 18, dimethyl-dioctadecyl ammonium bromide, and the polyene antibiotics, Nystatin and Amphotericin B). None of these **adjuvants** were as effective as saponin, although FCA, Al(OH)3 and C. parvum augmented immunity considerably. The possible reasons for the efficacy of saponin as an **adjuvant** for protozoal vaccines are discussed. The P. yoelli/mouse system provides a sensitive and rapid screening assay for

comparison of potential **adjuvants** suitable for use with a malaria vaccine.

L7 ANSWER 82 OF 103 CAPLUS COPYRIGHT 2000 ACS
1983:83349 Document No. 98:83349 Enhancement of delayed-type hypersensitivity and induction of interferon by the lipophilic agents DDA and CP 20961. Kraaijeveld, Cornelis A.; Snippe, Harm; Harmsen, Theo; Benaissa-Trouw, Barry (Lab. Microbiol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Cell. Immunol., 74(2), 277-83 (English) 1982. CODEN: CLIMB8. ISSN: 0008-8749.
AB The lipophilic amines dimethyl dioctadecyl ammonium bromide (DDA) [**3700-67-2**] and N,N-dioctadecyl-N',N'-bis(2-hydroxyethyl)propanediamine (CP 20961) [35607-20-6] are compared on their capacities to induce interferon, nonspecific protection to viral infection, and enhancement of delayed-type hypersensitivity (DH). DDA, a well-known **adjuvant** for the induction of DH is a moderate interferon inducer like CP 20961. On the other hand, CP 20961, a known interferon inducer and resembling in structure DDA, is shown to enhance DH to inactivated Semliki Forest virus . Nonspecific protection to challenge with a LD of either SFC or encephalomyocarditis virus was induced on injection of both compds.

L7 ANSWER 83 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 36
1982:215660 Document No. 96:215660 Adjuvanticity of dimethyl dioctadecyl ammonium bromide in guinea pigs. I. Skin test reactions. Snippe, Harm; De Reuver, Marinus J.; Kamperdijk, Ed. W. A.; Van den Berg, Marja; Willers, Jan M. N. (Dep. Immunol., State Univ. Utrecht, Utrecht, 3511GG, Neth.). Int. Arch. Allergy Appl. Immunol., 68(3), 201-8 (English) 1982. CODEN: IAAAAM. ISSN: 0020-5915.
AB The effect of the **adjuvant** dimethyl dioctadecyl ammonium bromide (DDA) on the induction of cellular immunity in guinea pigs was studied. DDA, a surface-active lipid, was mixed with the antigen bovine serum albumin (BSA) or with a conjugate of BSA and dinitrophenol (DNP22-BSA) and injected into the footpads of guinea pigs. At varying intervals skin tests were performed to test the immediate and delayed hypersensitivity (DH) reactions. Optimal DH reactions to BSA were obsd. from 3 to 6 wk after immunization with BSA in DDA. The hapten-specific response to DNP22-BSA had an optimum at 3 wk and was highly specific for the homologous antigen. Histol. examns. of skin test sites confirmed that the reaction was rather of the tuberculin type than of the cutaneous basophil hypersensitivity type. When guinea pigs were immunized with DNP22-BSA in Freund's complete **adjuvant** (FCA) a long-lasting DH to both carrier and hapten groups developed but the DH was always complicated by an Arthus reaction due to antibodies to the DNP hapten. Thus, DDA is superior to FCA as **adjuvant** for the induction of pure DH in guinea pigs.

L7 ANSWER 84 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 37
1982:249535 Document No.: BA74:22015. DELAYED HYPER SENSITIVITY IN RABBITS COMPARISON OF DI METHYL DIOCTADECYL AMMONIUM BROMIDE AND FREUNDS COMPLETE **ADJUVANT**. SNIPPE H; DE REUVER M J; BEUNDER J W; VAN DER MEER J B; VAN WICHEN D F; WILLERS J M N. DEP. OF IMMUNOL., LABORATORY OF MICROBIOL., CATHARIJNESINGEL 59, NL-3511 GG UTRECHT, THE NETHERLANDS.. INT ARCH

ALLERGY APPL IMMUNOL, (1982) 67 (2), 139-144. CODEN: IAAAAM. ISSN: 0020-5915. Language: English.

AB Injection of rabbits with antigen mixed with the cationic surface-active lipid dimethyl dioctadecyl ammonium bromide (DDA) induced delayed-type hypersensitivity (DH), which could be measured as skin reactions and was confirmed by histology of the skin test sites. One wk after injection of a conjugate of bovine serum albumin (BSA) with dinitrophenol (DNP30-BSA) mixed with DDA, DH was detectable in most but not in all rabbits. Similar results were obtained using FCA [Freund's complete **adjuvant**] as **adjuvant**. The animals treated with FCA produced a long-lasting DH (1-3 wk) complicated by circulating anti-DNP antibodies (Arthus-type reactions). Skin testing with heterologous hapten-carrier complexes revealed that individual rabbits immunized with DNP30-BSA in DDA expressed DH with different reaction patterns, either to hapten, carrier or both. DDA is a useful **adjuvant** for the induction of a state of pure DH in rabbits. Not all rabbits do respond, or respond similarly.

L7 ANSWER 85 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS

1981:104021 Document No.: BR21:39017. A CHEMICALLY DEFINED IMMUNOLOGIC **ADJUVANT** DI METHYL DIOCTADECYL AMMONIUM BROMIDE. BAECHTEL F S; GORDON W C; MAULDIN S; PRAGER M D. UNIV. TEX. HEALTH SCI. CENT., DALLAS, TEX. 75235, USA.. 65TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GA., USA, APRIL 12-17, 1981. FED PROC. (1981) 40 (3 PART 2), 1151. CODEN: FEPRA7. ISSN: 0014-9446. Language: English.

L7 ANSWER 86 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS

1981:79785 Document No.: BR21:14781. INDUCTION OF A CELL MEDIATED IMMUNE RESPONSE TO BRUCELLA-ABORTUS WITHOUT CONCOMITANT ANTIBODY. FRENCHICK P J; JOHNSON D W; MUSCOPLAT C C. UNIV. MINN., ST. PAUL, MINN. 55108, USA.. 65TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, ATLANTA, GA., USA, APRIL 12-17, 1981. FED PROC. (1981) 40 (3 PART 2), 1123. CODEN: FEPRA7. ISSN: 0014-9446. Language: English.

L7 ANSWER 87 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS

1982:216042 Document No.: BA73:76026. CHARACTERIZATION OF IMMUNOGENIC PROPERTIES OF HAPTENATED LIPOSOMAL MODEL MEMBRANES IN MICE 5. EFFECT OF MEMBRANE COMPOSITION ON HUMORAL AND CELLULAR IMMUNOGENICITY. VAN HOUTE A J; SNIPPE H; SCHMITZ M G J; WILLERS J M N. DEP. OF IMMUNOLOGY, LABORATORY OF MICROBIOLOGY, CATHARIJNESINGEL 59, 3511 UTRECHT, THE NETHERLANDS.. IMMUNOLOGY, (1981) 44 (3), 561-568. CODEN: IMMUAM. ISSN: 0019-2805. Language: English.

AB The effect of altering liposomal membrane composition on humoral and cellular immunogenicity of haptenated liposomes in mice is described. Antibody formation was determined by enumeration of direct, plaque-forming cells in the spleen and delayed hypersensitivity (DH) was measured with a footpad swelling test. Humoral immunogenicity of haptenated liposomes was strongly influenced by membrane phospholipid, cholesterol and charged amphiphile composition. Haptenated liposomes prepared from phospholipids with a low (dioleoyl- and dilauroyl-phosphatidylcholine) or high (distearoyl phosphatidylcholine) phase-transition temperature were less immunogenic than those prepared from phospholipids with an intermediate phase-transition temperature (dipalmitoyl phosphatidylcholine and sphingomyelin). Increasing the amount of liposomal membrane cholesterol generally induced a higher humoral response. Results are discussed in relation to liposomal membrane fluidity. Induction of an optimal DH with

haptenated liposomes did not occur in the absence of the **adjuvant** dimethyl dioctadecyl ammonium bromide (DDA). When DDA was used, alterations in membrane composition did not influence cellular immunogenicity. Intermediate liposomal membrane fluidity is apparently the most important requirement for induction of optimal antibody formation with haptenated liposomes. A certain physicochemical configuration of the antigen, provided by the **adjuvant** DDA, is probably a prerequisite for induction of DH.

L7 ANSWER 88 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
81174576 EMBASE Document No.: 1981174576. **Adjuvant** effect of nonionic block polymer surfactants in humoral and cellular immunity. Snippe H.; De Reuver M.J.; Strickland F.; et al.. Dept. Immunol., Lab. Microbiol., State Univ., Utrecht 3511GG, United States. International Archives of Allergy and Applied Immunology 65/4 (390-398) 1981. CODEN: IAAAAM. Pub. Country: Switzerland. Language: English.

AB The **adjuvant** activities of four chemically similar, but physicochemically different nonionic suface-active agents called pluronic polyols F 68, L 31, L 101 and L 121 were studied. These four agents were tested in mice using an experimental model developed for studying the **adjuvant** activity of the cationic surface-active agent dimethyl dioctadecyl ammonium bromide (DDA). L 121 and DDA enhanced the primary antibody response to sheep red blood cells (SRBC) while F 68, L 31 and L 101 suppressed this response. The secondary humoral response to SRBC was enhanced by the polyol L 121 while the secondary response to dinitrophenylated bovine serum albumin (DNP22-BSA) was enhanced by both L 121 and L 101. DDA and the polyol L 101 were very effective **adjuvants** for induction of delayed-type hypersensitivity (DTH) to SRBC and DNP22-BSA after intracutaneous immunization of mice with a mixture of antigen and **adjuvant**. Since the four pluronic polyols were composed of identical chemical constituents, we proposed that difference in their activities as **adjuvants** were due to variation in their physicochemical properties. A correlation was found between a physicochemical parameter, the hydrophile-lipophile balance (HLB), and the **adjuvant** activities of the pluronic polyols and several other types of nonionic surface-active agents. The agents which were strong **adjuvants** all had HLB values within a narrow range which classified them as spreading agents.

L7 ANSWER 89 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1980:87659 Document No.: BR19:25157. EFFECT OF OILS AND SURFACTANTS ON THE HUMORAL AND CELLULAR IMMUNE RESPONSE. STRICKLAND F; PELLEY R P; HUNTER R L. PATHOL. DEP., UNIV. CHIC., 950 E. 59TH ST., CHICAGO, ILL. 60637, USA.. 64TH ANNUAL MEETING OF THE FED. AM. SOC. EXP. BIOL., ANAHEIM, CALIF., USA, APR. 13-18, 1980. FED PROC. (1980) 39 (3), ABSTRACT 2173. CODEN: FEPRA7. ISSN: 0014-9446. Language: English.

L7 ANSWER 90 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1980:77385 Document No.: BR19:14883. VARIABLE EXPRESSION OF DELAYED HYPER SENSITIVITY IN DIFFERENT MOUSE STRAINS USING DI METHYL DI OCTADECYL AMMONIUM BROMIDE AS AN **ADJUVANT**. SNIPPE H; SCHOTT C; MERCHANT B. FOOD DRUG ADM.-BUR. BIOL., ROOM 225, 8800 ROCKVILLE PIKE, BETHESDA, MD. 20205, USA.. 64TH ANNUAL MEETING OF THE FED. AM. SOC. EXP. BIOL., ANAHEIM, CALIF., USA, APR. 13-18, 1980. FED PROC. (1980) 39 (3), ABSTRACT 1119. CODEN: FEPRA7. ISSN: 0014-9446. Language: English.

L7 ANSWER 91 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1981:134334 Document No.: BA71:4326. SPECIFIC IMMUNO PROPHYLAXIS IN

EXPERIMENTAL TUMOR HOST SYSTEMS. PRAGER M D; GORDON W C. DEP. SURG., UNIV.
TEX. HEALTH SCI. CENT., 5323 HARRY HINES BLVD., DALLAS, TEX. 75235, USA.. CAN MED ASSOC J, (1980) 122 (7), 780-784. CODEN: CMAJAX. ISSN: 0008-4409. Language: English.

AB A variety of animal species have been rendered resistant to syngeneic tumors of many histologic types by immunoprophylaxis. Among the types of preparation of tumor-associated antigens that have merit as vaccines are tumor cells treated with radiation, mitomycin C, certain viruses, neuraminidase, SH blocking agents and lipoidal reagents. Tumor-associated antigens of the cell membrane may be solubilized and used for vaccination.

Dimethyldioctadecylammonium bromide modifies tumor cells [mouse leukemia L-1210 cells and mouse lymphoma cells (6C3HED, P1798, YAC)] and serves as an immunologic **adjuvant**; it enhances protective responses to iodoacetamide-treated lymphoma cells and acts as a potent macrophage activator. By judicious application of DDA, delayed hypersensitivity or antibody response may be selectively enhanced. Advantages of DDA over other **adjuvants** are as follows: it is water soluble; it does not produce deleterious lesions at the site of injection; it eliminates the risk of systemic infection that exists with the use of live bacteria.

L7 ANSWER 92 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1981:168462 Document No.: BA71:38454. COMPARISON OF MURAMYL DI PEPTIDE TREHALOSE DI MYCOLATE AND DI METHYL DI OCTA DECYL AMMONIUM BROMIDE AS **ADJUVANTS** IN BRUCELLA-ABORTUS 45-20 VACCINES. WOODARD L F; TOONE N M; MCLAUGHLIN C A. DEP. OF VETERINARY SCI., UNIV. OF IDAHO, MOSCOW, IDAHO 83843.. INFECT IMMUN, (1980) 30 (2), 409-412. CODEN: INFIBR. ISSN: 0019-9567. Language: English.

AB The capacity of trehalose dimycolate (TDM), muramyl dipeptide (MDP) and dimethyl dioctadecyl ammonium bromide (DDA), alone or in combination, to potentiate the immunogenicity of killed B. abortus 45/20 bacteria was studied in guinea pigs. Bacterins that contained TDM in oil droplet emulsion were as effective in the prevention of brucellosis as those emulsified in Freund complete **adjuvant**; bacterins that contained a combination of TDM and MDP were most effective. Vaccinal emulsions of bacteria and MDP were ineffective in the prevention of splenic infections.

DDA was unable to potentiate acquired resistance to Brucella. Addition of DDA to 1% oil emulsions of bacteria, TDM and MDP eliminated protection. **Adjuvants** without bacteria were not able to nonspecifically protect animals from infection, although TDM was able to significantly reduce the numbers of splenic Brucella. A positive correlation ($P < 0.0001$) between splenic infection and splenic weight was found.

L7 ANSWER 93 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 38
1980:405776 Document No. 93:5776 Variable expression of delayed hypersensitivity in different mouse strains using dimethyl dioctadecyl ammonium bromide as an **adjuvant**. Snippe, H.; Johannesen, L.; Lizzio, Elaine; Merchant, B. (Div. Blood Blood Prod., Bur. Biol. Food Drug Adm., Bethesda, MD, USA). Immunology, 39(3), 399-405 (English) 1980. CODEN: IMMUAM. ISSN: 0019-2805.

AB Delayed-type hypersensitivity measured as footpad swelling was produced in inbred mouse strains with the 2,4-dinitrophenyl-bovine serum albumin complex mixed with di-Me dioctadecyl ammonium bromide; great variation was obsd. in delayed hypersensitivity among different mouse strains. The highest responding animals were BALB/cJ mice, the lowest were P/JN and outbred nu/nu mice. No correlation was obsd. between H-2 type and the

intensity of the elicited reactions.

L7 ANSWER 94 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 39
1980:424195 Document No. 93:24195 The specificity of antibody formation in mice following immunization with hapten-carrier complexes mixed with the surfactant, dimethyl dioctadecyl ammonium bromide. Snippe, H.; Willers, J. M. N.; Inman, J. K.; Merchant, B. (Dep. Immunol. Lab. Microbiol., State Univ. Utrecht, Utrecht, 3511 GG, Neth.). Immunology, 39(3), 361-6 (English) 1980. CODEN: IMMUAM. ISSN: 0019-2805.
AB Delayed-type hypersensitivity (DH) was generated in mice immunized with hapten-carrier complexes mixed with **adjuvant** di-Me dioctadecyl ammonium bromide. Both direct and indirect hapten-specific plaque forming cells were, however, detected in peripheral lymph nodes and spleen 4 days after challenge. Although the **adjuvant** promoted a strong crossreactivity in DH between heterol. hapten-carrier complexes, the antibody-forming cells produced 4 days after challenge showed relatively high specificity for the immunizing antigen. The possibility existed, therefore, that B-cell receptors may be capable of expressing a greater degree of hapten specificity than T-cell receptors. Thus, Thelper cells participating in antibody formation may represent a subset of the T cells involved in DH.

L7 ANSWER 95 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 40
1980:69682 Document No. 92:69682 The enhancement of humoral and cellular immune responses by dimethyldioctadecylammonium bromide. Gordon, William C.; Prager, Morton D.; Carroll, Michael C. (Southwest. Med. Sch., Univ. Texas, Dallas, TX, 75235, USA). Cell. Immunol., 49(2), 329-40 (English) 1980. CODEN: CLIMB8. ISSN: 0008-8749.
AB Dimethyldioctadecylammonium bromide (DDA) [**3700-67-2**] produced marked enhancement of both cellular and humoral immune responses to sheep red blood cells (SRBC) when administered to mice i.p., or of cellular immunity when given s.c. Stimulated cellular responses were seen as increased footpad swelling as a measure of delayed hypersensitivity and increased antigen-induced blastogenesis. Elevation of humoral response was reflected in increased nos. of splenic plaque-forming cells (PFC) and in circulating anti-SRBC antibody. Adjuvancy did not depend on addn. of the lipid of DDA to antigen, as both humoral and cellular responses were enhanced whether DDA and SRBC were admixed or injected sep. 4 h apart i.p. DDA also enhanced the PFC response to the T-cell independent antigen trinitrophenylated lipopolysaccharide (TNP-LPS). The DDA effects were accompanied by macrophage activation, which may mediate at least in part the obsd. responses. DDA-activated macrophages exhibit fast spreading, are highly phagocytic, and elaborate significantly greater amts. of thymocyte mitogenic factor(s) than do normal resident peritoneal macrophages. This activation may effect the stimulation of antigen-specific primary lymphocyte responses by **adjuvant** and expansion of memory-cell populations which lead to the obsd. enhancement of secondary responses.

L7 ANSWER 96 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1981:58926 Document No.: BR20:58926. SESSION ON TRANSPLANTATION IMMUNOLOGY 2. INDUCTION OF SPECIFIC TRANSPLANTATION TOLERANCE IN MAN BY AUTO BLAST IMMUNIZATION. CHAMBERS J D; THOMAS C R; HOBBS J R. DEP. CHEM. PATHOL., WESTMINSTER MED. SCH., PAGE ST., LONDON SW1P 2AR, G.B.. ANNUAL MEETING OF THE EUROPEAN FOUNDATION FOR BONE MARROW TRANSPLANTATION, ENGADINE, SWITZERLAND, APRIL 13-16, 1980. BLUT. (1980) 41 (3), 229-236. CODEN: BLUTA9. ISSN: 0006-5242. Language: English.

L7 ANSWER 97 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1981:154550 Document No.: BA71:24542. DI METHYLDIOCTADECYL AMMONIUM BROMIDE AS
AN **ADJUVANT** FOR DELAYED TYPE HYPER SENSITIVITY AND CELLULAR IMMUNITY AGAINST SEMLIKI-FOREST VIRUS IN MICE. KRAAIJEVELD C A; SNIPPE H; HARMSEN M; BOUTAHAR-TROUW B K. RIJKSUNIV. UTRECHT, LAB. MICROBIOL., CATHARIJNESINGEL 59, 3511 GG UTRECHT, NETH.. ARCH VIROL, (1980) 65 (3-4), 211-218. CODEN: ARVIDF. ISSN: 0304-8608. Language: English.
AB Intracutaneous immunization of BALB/c mice with inactivated Semliki Forest
virus mixed with the cationic, surface active lipid dimethyldioctadecyl ammonium bromide produced a strong enhancement of delayed type hypersensitivity without detectable antibodies in serum. These mice were more protected against i.p. challenge than normal immunized mice. This protection might be explained by an enhancement of cellular immunity against Semliki Forest virus. Dimethyldioctadecyl ammonium bromide by itself has no effect on footpad swelling, mortality and mean survival time.

L7 ANSWER 98 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 41
1981:13946 Document No. 94:13946 Saponin and other hemolysins (vitamin A, aliphatic amines, polyene antibiotics) as **adjuvants** for SRBC in the mouse. Evidence for a role for cholesterol-binding in saponin adjuvanticity. Bomford, R. (Dep. Exp. Immunobiol., Wellcome Res. Lab., Beckenham/Kent, Engl.). Int. Arch. Allergy Appl. Immunol., 63(2), 170-7 (English) 1980. CODEN: IAAAAM. ISSN: 0020-5915.
AB The hypothesis that the **adjuvant**, as well as the hemolytic, activity of saponin depends on binding to cholesterol in cell membranes is
supported by showing that cholesterol absorbs out **adjuvant** activity, and inhibits immunopotentiation in vivo when added to the injection mixt. Also, out of a range of hemolytic substances, chosen for their known properties as **adjuvants** or for cholesterol binding, the only materials which displayed a comparable activity to saponin were the polyene antibiotics nystatin and amphotericin B, whose binding to membrane cholesterol causes similar morphol. changes to that of saponin.

L7 ANSWER 99 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 42
1980:108968 Document No. 92:108968 Effect of selenium and dimethyl dioctadecyl ammonium bromide on the vaccine-induced immunity of Swiss-Webster mice against malaria (Plasmodium berghei). Desowitz, Robert
S.; Barnwell, John W. (John A. Burns Sch. Med., Univ. of Hawaii, Honolulu,
HI, 96816, USA). Infect. Immun., 27(1), 87-9 (English) 1980. CODEN: INFIBR. ISSN: 0019-9567.
AB Se, as sodium selenite, at a concn. of 2.5 .mu.g/Se/mL administered in drinking water, potentiated the protective effect of a killed P. berghei vaccine for Swiss-Webster mice. A vaccine consisting of P. berghei antigen combined with the **adjuvant**, dimethyl dioctadecyl ammonium bromide (I), conferred a significantly high level of protective immunity. An additive effect was shown in that the greatest degree of protection was afforded to the group of mice maintained on Se and vaccinated with antigen-I. Almost all of the animals treated in this manner survived the challenging infection, the course of which was typically of a transitory parasitemia not >10% at the peak.

L7 ANSWER 100 OF 103 BIOSIS COPYRIGHT 2000 BIOSIS
1979:251296 Document No.: BA68:53800. DELAYED TYPE HYPER SENSITIVITY AND ACQUIRED CELLULAR RESISTANCE IN MICE IMMUNIZED WITH KILLED LISTERIA-MONOCYTOGENES AND **ADJUVANTS**. VAN DER MEER C; HOFHUIS F

M A; WILLERS J M N. DEP. IMMUNOL. LAB. MICROB., CATHARIJNESINGEL 59, 3511 GG UTRECHT, NETH.. IMMUNOLOGY, (1979) 37 (1), 77-82. CODEN: IMMUAM. ISSN: 0019-2805. Language: English.

AB Delayed-type hypersensitivity (DH) and acquired cellular resistance (ACR) to L. monocytogenes in mice was studied following immunization with killed bacteria in combination with Freund's complete **adjuvant** [FCA] or the **adjuvant** dimethyldioctadecylammonium bromide (DDA). Intracutaneous or i.p. injections of killed Listeria mixed with FCA resulted neither in DH nor in ACR. Intracutaneous injections of killed Listeria and DDA resulted in an antigen-dose dependent DH but not in ACR. Injection of Listeria and DDA i.p. induced ACR but no DH. Optimal conditions for the induction of ACR were simultaneous i.p. injection of 15 mg DDA/kg body wt and 107 or 108 Listeria. The optimal interval between immunization and challenge was 7 days. No protection was found against challenge with a lethal dose of Salmonella enteritidis, suggesting that the protection is specific. Injection of mice with DDA i.p. resulted in inhibition of phagosome-lysosome fusion in macrophages harvested 24 h later. Interference with macrophage activity is discussed as a possible mechanism for the **adjuvant** effect of DDA.

L7 ANSWER 101 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 43

1979:20667 Document No. 90:20667 **Adjuvant** effect of cationic surface-active lipid, dimethyl dioctadecyl ammonium bromide, on the induction of delayed-type hypersensitivity to sheep red blood cells in mice. Chiba, Joe; Egashira, Yasuyuki (Dep. Pathol., NIH, Tokyo, Japan). Jpn. J. Med. Sci. Biol., 31(4), 361-4 (English) 1978. CODEN: JJMCAQ. ISSN: 0021-5112.

AB The **adjuvant** effect of di-Me dioctadecyl ammonium bromide (DDA) on the induction of delayed-type hypersensitivity (DTH) to sheep red blood cells (SRBC) in mice was examd. Markedly enhanced DTH to SRBC was induced by s.c. injection of 2 .times. 108 SRBC suspended in saline contg. 1 mg/mL DDA as compared to DTH responses in control animals sensitized with the same doses of SRBC without DDA. The enhancement of DTH responses seemed closely related to the delayed appearance of circulating antibody to SRBC and not to the strain or the age of mice.

L7 ANSWER 102 OF 103 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

78309248 EMBASE Document No.: 1978309248. Use of a lipid **adjuvant** in chemoimmunotherapy. Prager M.D.; Gordon W.C.. Univ. Texas Hlth. Sci. Cent., Dallas, Tex. 75235, United States. Proceedings of the American Association for Cancer Research Vol. 19/- (no.318) 1978. CODEN: PAACA3. Pub. Country: United States. Language: English.

L7 ANSWER 103 OF 103 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 44

1978:168333 Document No. 88:168333 Dimethyl dioctadecyl ammonium bromide as **adjuvant** for delayed hypersensitivity in mice. Snippe, H.; Belder, Margriet; Willers, J. M. N. (Dep. Immunol., State Univ., Utrecht, Neth.). Immunology, 33(6), 931-6 (English) 1977. CODEN: IMMUAM. ISSN: 0019-2805.

AB The delayed hypersensitivity (DH) responses to sheep red blood cells or dinitrophenylated bovine serum albumin (DNP28-BSA) in di-Me dioctadecyl ammonium bromide (I) exceeded those in Freund's complete **adjuvant** (FCA). Pretreatment with cyclophosphamide (300 mg/kg, i.p.) 8 h before immunization with antigen in FCA or I delayed the onset of DH and eliminated the differences in the response due to the **adjuvants**. The DH to DNP28-BSA was DNP-specific. Peak responses to in vivo priming

with DNP28-BSA in I and in vitro stimulation with the same antigen were twice as high and were reached twice as fast as those following immunization in FCA. The advantages of I as **adjuvant** over covalently linked fatty acid chains and over FCA are discussed.

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